Special Foods Subcommittee of the Pharmacology and Therapeutics Advisory Committee (PTAC)

Meeting held on 7 December 2017

(minutes for web publishing)

Special Foods 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 Special Foods Subcommittee meeting; the relevant portions of the minutes relating to Special Foods Subcommittee discussions about an Application or PHARMAC staff proposal that contain a recommendation are generally published.

The Special Foods 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 was reviewed by PTAC at its meeting on 3 & 4 May 2018, the record of which will be available in due course.

Record of the Special Foods Subcommittee meeting held at Bell Gully Offices on 7 December 2017

1 Record of previous minutes

1.1 The Subcommittee noted the record of the previous meeting that took place on 22 July 2015. The Subcommittee considered that there were incorrect statements that required amendment. The incorrect minute(s), listed below, followed by reason for amending and the suggested minute.

1.2 The Subcommittee discussed the minute below and considered that it was incorrect as biologic treatment was not the appropriate comparator. The Subcommittee considered that 'biologic treatment' should be replaced with 'steroid treatment'.

> *6.17 The Subcommittee noted that EEN for children with Crohn's disease has been ranked against other funding options PHARMAC has. The Subcommittee considered that EEN reduces the need for the progression to treatment with biologics. The Subcommittee recommended that biologic treatment be used as the appropriate comparator.*

1.3 The Subcommittee considered that the above minute should be amended to read:

> *6.17 The Subcommittee noted that EEN for children with Crohn's disease has been ranked against other funding options PHARMAC has. The Subcommittee considered that EEN reduces the need for the progression to treatment with biologics. The Subcommittee recommended that steroid treatment be used as the appropriate comparator.*

1.4 The Subcommittee considered that the remaining minutes were an accurate record of the meeting that took place on 22 July 2015.

2 Updated NPPA policy

2.1 The Subcommittee noted a presentation by PHARMAC staff on the updated Exceptional Circumstances framework and the updated Named Patient Pharmaceutical Assessment (NPPA) application process online.

2.2 The Subcommittee noted that there was no clear definition for how unique a patient needed to be to be considered for funded treatments via the NPPA process, under the NPPA policy's exceptional clinical circumstances principle.

2.3 The Subcommittee noted that evidence of efficacy for a non-funded treatment through a patient self-funded trial or a compassionate supply by a supplier was not considered by NPPA during the assessment. The Subcommittee also noted information from PHARMAC staff that this may create an inequity of access due to some patients not being in a position to trial a treatment first. Members considered that while this rationale was understandable, it was also important to consider evidence from a real-world-setting as part of the NPPA assessment process.

2.4 The Subcommittee noted that the new online NPPA application form did not remind clinicians to obtain consent from their patients prior to sending their personal information

to PHARMAC. The Subcommittee noted this reminder was on the NPPA Word document form.

3 Factors for Consideration

3.1 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.

3.2 The Subcommittee considered that the wheel presentation of the FFC was an improvement over the previous nine Decision Criteria list.

4 Therapeutic Group Review

4.1 The Subcommittee noted that overall the Special Foods Therapeutic group was experiencing significant growth mainly borne out of the Oral Supplements therapeutic area. The Subcommittee considered that for patients commencing on an oral supplement there is not adequate criteria in place to encourage them to re-trial food.

1. Therapeutic Group Review Summary

Food thickeners

4.2 The Subcommittee noted that Since 2014 there has been an increase in prescriptions for food thickeners in the community. Members considered that this number of patients did not correlate to those with motor neurone disease and who had swallowing disorder and was more reflective of a wider patient group with disordered swallowing of any cause.

4.3 The Subcommittee noted its 2015 advice on this matter, members considered that its recommendation to delist food thickeners in the community was still its current viewpoint. While food thickeners still remain listed in the community, the Subcommittee considered that limiting Special Authority applications to neurologists or on the recommendation of a neurologist would help to reduce inappropriate use. The Subcommittee **recommended** the following changes to the Special Authority (additions in bold, deletions in strikethrough):

> **Initial** application only from a ~~dietitian, relevant specialist or vocationally registered general practitioner~~ **neurologist or medical practitioner on the recommendation of a neurologist**. Approvals valid for 1 year where the patient has motor neurone disease with swallowing disorder.
>
> **Renewal** only from a ~~dietitian, relevant specialist, vocationally registered general practitioner or general practitioner on the recommendation of a dietitian, relevant specialist or vocationally registered general practitioner~~ **neurologist or medical practitioner on the recommendation of a neurologist.**
> Approvals valid for 1 year for applications meeting the following criteria:
> Both:
> 1 The treatment remains appropriate and the patient is benefiting from treatment; and
> 2 ~~General Practitioners~~ **Medical practitioners** must include the name of the ~~dietitian, relevant specialist or vocationally registered general practitioner~~ **neurologist** and date contacted.

4.4 The Subcommittee noted that pre-thickened drinks and supplements included in Section H had a note that stipulated that access for named patients' needs to have been

established prior to 1 July 2013. The Subcommittee noted that this note may have been interpreted as meaning for ward use and was not being interpreted as patient specific use. The Subcommittee considered that the ward use pre-thickened drinks and supplements in the Hospital should have the input of a speech and language therapist and therefore an amendment to this note should be made to reflect this. The Subcommittee **recommended** the following changes to the note in the HML regarding Food/Fluid Thickeners (additions in bold, deletions in strikethrough):

> **NOTE**:
> While pre-thickened drinks and supplements have not been included in Section H, DHB hospitals may continue to use such products for patients with dysphagia, provided that:
> • ~~use was established prior to 1 July 2013~~ **Individual patient or ward use had been established under the guidance of a speech and language therapist; and**
> • the product has not been specifically considered and excluded by PHARMAC; and
> • use of the product conforms to any applicable indication restrictions for similar products that are listed in Section H (for example, use of thickened high protein products should be in line with the restriction for high protein oral feed in Section H).
> PHARMAC intends to make a further decision in relation to pre-thickened drinks and supplements in the future, and will notify of any change to this situation.

Foods and supplements for inborn errors of metabolism

4.5 The Subcommittee noted that foods and supplements for inborn errors of metabolism category had seen some market growth over the last five years. Members considered that overall expenditure is predominately from 'supplements for PKU' of which there are approximately 100 scripted patients in New Zealand. Members considered that the incidence of PKU in New Zealand is stable. However, Members noted that since the introduction of newborn screening of PKU the average age of PKU patients has increased and correspondingly so has consumption.

4.6 The Subcommittee considered that some patients on a PKU diet struggle with adherence and while this is not solely due to the range of protein supplements made available to them, range is a contributing factor. One member explained how much phenylalanine is contained in a product would determine how much free proteins (from other foods) a patient can eat which also impacts variety for patients and can improve compliance. Members considered that 40-50% of scripted patients do not achieve target phenylalanine levels which can have varying neurological impacts depending on age of patients and other unknown factors.

4.7 Members consider that there is a high cost per patient relative to other specialised feeds and that PHARMAC could consider a competitive process in this therapeutic space. Members considered that careful consideration would need to go into a competitive process in this patient group who struggle with treatment adherence, in some part due to taste fatigue from the small range of PKU products available in New Zealand. Members considered there would be some increase in usage from having a larger range of PKU products, this increase would need to be considered as part of the RFP evaluation. Members considered a dual supply arrangement would allow an additional range of products available to these patients. Members also considered that consumer input into the competitive process to assess taste would be advantageous.

Gluten free foods

4.8 The Subcommittee noted that PHARMAC does not actively manage gluten free foods. Members considered that this is appropriate as there is a significant range of gluten free foods available at retail outlets.

4.9 Members noted correspondence from Auckland DHB regarding the Special Authority requiring that the diagnosis of Gluten enteropathy has been diagnosed by biopsy. This correspondence considered that the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) guidelines stipulate that in selected children who fulfil certain rigorous criteria, a biopsy diagnosis for coeliac disease is not required and that the diagnosis can be made on history of symptoms, significantly elevated serology and HLA testing alone. Members considered that measuring blood levels may have the potential for increasing the patient population eligible if it captured slightly raised antibody levels. Members considered that this request would be more appropriately considered by the Gastrointestinal Subcommittee, and should be forwarded this correspondence for their consideration.

Infant formula

4.10 The Subcommittee noted at its July 2015 meeting a recommendation was made to review initial and renewal amino acid formula (AAF) applications via a Panel for patients over 12 months due to high expenditure in this group. Members noted feedback from PHARMAC on the issues surrounding such a recommendation including cost, patient numbers and additional prescriber burden involved in applications.

4.11 Members considered that many patients are prescribed AAF inappropriately, when an extensively hydrolysed formula would be effective. Members also considered that patients are kept on formula for too long when they should have been progressed to solids from six months of age. Members considered that the patient group that are on AAF and are over 12 months of age should be small, with complicated disease, and all of these patients would be under the care of a paediatric immunologist, gastroenterologist or general paediatrician.

4.12 The Subcommittee considered that the current Special Authority for AAF criteria requires that patients have reasonably trialled eHF and have a history of documented severe intolerance, allergy, malabsorption, a history of anaphylaxis to cows milk protein formula or dairy products or eosinophilic oesophagitis. Members considered that General Practitioners are not trained in the diagnosis, ruling-out and management of patients with these conditions. Members considered that it would be inequitable however to restrict all initial applications for AAF to specialist care. Members considered that from 12 months of age patients that had a severe gastrointestinal condition would have been able to have an appointment with either a general paediatrician or paediatric immunologist or gastroenterologist and therefore considered that the Special Authority criteria could be split into two groups, patients under 12 months of age and patients over 12 months of age.

4.13 The Subcommittee **recommended** changes to the Special Authority criteria for AAF that maintained current patient access under the age of 12 months while putting in place restriction for those over 12 months of age; this restriction was that if over the age of 12 months the patient be required to have been reviewed by a prescriber trained in managing patients with severe immunological or gastrointestinal issues. Members also noted that patients over 12 months of age should have a longer Special Authority expiry that reflects access to specialist care and the requirement for less frequent review of

treatment. Members **recommended** the following new Special Authority for AAF (additions in bold, deletions ins strikethrough):

Initial application - (**Infants up to 12 months of age)** only from a dietitian, **paediatrician** or vocationally registered general practitioner. Approvals valid for 6 months for applications meeting the following criteria:
Any of the following:

1 History of anaphylaxis to cows milk protein formula or dairy products**; or**
2 Eosinophilic oesophagitis**; or**
3 Ultra-short gut; or
4 Severe Immune deficiency; or
5 Both:
5.1 Extensively hydrolysed formula has been reasonably trialled **for 2-4 weeks (for non IgE mediated)** and is inappropriate due to documented severe intolerance or allergy or malabsorption; and
5.2 Either:
5.2.1 Both:
5.2.1.1 The patient has a valid Special Authority approval for extensively hydrolysed formula; and
5.2.1.2 Either:
5.2.1.2.1 Patient has IgE mediated allergy; or
5.2.1.2.2 Patient has non IgE mediated severe gastrointestinal intolerance; or
5.2.2 Extensively hydrolysed formula has been trialled in an inpatient setting.

Initial application - **(Children over 12 months of age**) only from a **paediatrician**. Approvals valid for **12** months for applications meeting the following criteria:
Any of the following:

1 History of anaphylaxis to cows milk protein formula or dairy products**; or**
2 Eosinophilic oesophagitis**; or**
3 Ultra-short gut; or
4 Severe Immune deficiency; or
5 Both:
5.1 Extensively hydrolysed formula has been reasonably trialled **for 2-4 weeks (for non IgE mediated)** and is inappropriate due to documented severe intolerance or allergy or malabsorption; and
5.2 Either:
5.2.1 Both:
5.2.1.1 The patient has a valid Special Authority approval for extensively hydrolysed formula; and
5.2.1.2 Either:
5.2.1.2.1 Patient has IgE mediated allergy; or
5.2.1.2.2 Patient has non IgE mediated severe gastrointestinal intolerance; or
5.2.2 Extensively hydrolysed formula has been trialled in an inpatient setting.

Renewal - (**Infants up to 12 months of age**) only from a dietitian, **paediatrician**, vocationally registered general practitioner or general practitioner on the recommendation of a dietitian, **paediatrician** or vocationally registered general practitioner. Approvals valid for 6 months for applications meeting the following criteria:
Either:

1 Patient has IgE mediated allergy
1.1 All of the following:
1.1.1 Patient remains allergic to cows milk; and
1.1.2 An assessment as to whether the infant can be transitioned to a soy or extensively hydrolysed infant formula has been undertaken; and
1.1.3 The outcome of the assessment is that the infant continues to require an amino acid infant formula; and
1.1.4 Amino acid formula is required for a nutritional deficit; and
1.1.5 General Practitioners must include the name of the dietitian, **paediatrician** or vocationally registered general practitioner and date contacted; and
1.1.6 This application is greater than three months from the previous approval; or

2 Patient has non IgE mediated severe gastrointestinal intolerance (including eosinophilic oesophagitis, Ultra-short gut and severe immune deficiency)

2.2 2.1 All of the following:

2.2.1 An assessment as to whether the infant can be transitioned to a cows milk protein, soy, or extensively hydrolysed infant formula has been undertaken; and

2.2.2 The outcome of the assessment is that the infant continues to require an amino acid infant formula; and

2.2.3 Amino acid formula is required for a nutritional deficit; and

2.2.4 General Practitioners must include the name of the dietitian, **paediatrician** or vocationally registered general practitioner and date contacted; and

2.2.5 This application is greater than three months from the previous approval.

Renewal - (**Children over 12 months of age**) only from a **paediatrician**. Approvals valid for **12** months for applications meeting the following criteria:

Either:

1 Both

1.1 Patient has IgE mediated allergy; and

1.2 All of the following:

1.2.1 Patient remains allergic to cows milk; and

1.2.2 An assessment as to whether the infant can be transitioned to a soy or extensively hydrolysed infant formula has been undertaken; and

1.2.3 The outcome of the assessment is that the infant continues to require an amino acid infant formula; and

1.2.4 Amino acid formula is required for a nutritional deficit; and

1.2.5 **This application is greater than six months from the previous approval**; or

2 Both:

2.1 Patient has non IgE mediated severe gastrointestinal intolerance; and

2.2 All of the following:

2.2.1 An assessment as to whether the infant can be transitioned to a cows milk protein, soy, or extensively hydrolysed infant formula has been undertaken; and

2.2.2 The outcome of the assessment is that the infant continues to require an amino acid infant formula; and

2.2.3 Amino acid formula is required for a nutritional deficit; and

2.2.4 This application is greater than six months from the previous approval.

Ketogenic diet

4.14 The Subcommittee noted that there are two DHBs that have dedicated teams for managing patients on Ketogenic diet Therapies (Auckland and Canterbury). Members noted that although there would be a theoretical potential for patient slippage for weight loss and parkinsons patients but there are limitations via prescriber restrictions and these should stay as metabolic physician or paediatric neurologist.

4.15 Members noted that 12-16 patients annually commence on a Ketogenic Diet Therapy at Starship Hospital and 10-30 at Christchurch Hospital are managed on a ketogenic diet. However the majority of KetoCal will be prescribed to tube fed Classical Ketogenic Diet Therapy patients. Patients are trialled for three months and if they respond (30-60% do), they continue on the diet for two years plus. Members considered that if other DHBs funded a service then numbers would increase relative to population in that area.

Nutrient modules

4.16 The Subcommittee noted that an observed trend of protein supplementation in nutrient modules are expected based on national guidelines to supplement first line with protein. Members considered that there is an increased trend for fat supplementation (Calogen and Liquigen) that is based on the 'Atkins' type of diet, noting also the downward trend of

carbohydrate supplementation. Members considered that PHARMAC should consider providing a report on usage of nutrient modules by age group and what other product in Section D of the Pharmaceutical Schedule they are being used with. Members considered that this could be reviewed at the next Subcommittee meeting to check if the rules are being followed.

Oral supplements/ complete diet (nasogastric/ gastrostomy tube feed)

4.17 The Subcommittee noted that oral supplements and complete diet make up 51% of the expenditure in the Special Foods Therapeutic Group. Members also noted that subsidy over the last five years has increased significantly (33%) due to a number of factors including wider prescriber access (general practice and dietitian prescribing in 2011). Members noted that following reference pricing of the sip feeds (1.5 kcal /ml RTDs) to the oral feed powders, a corresponding growth has been seen in the specialised oral feeds (paediatric oral feed, diabetic oral feed, renal oral feed, high calorie oral feed). Members considered that the Special Authority criteria for these feeds are likely too permissive and this has allowed patients that were faced with a part charge to continue on RTD standard oral supplements in 2011 to transition on to a fully funded specialised feeds at a higher cost.

Diabetic products

4.18 The Subcommittee noted that total diabetic product expenditure has grown 26% over the last five years, Members considered that this might be related to the aging population. Members considered that the Special Authority criteria is very permissive in that approvals are valid for one year. Patients need to be a type I or type II diabetic who are malnourished or underweight. Members considered that the criteria in place provides a long initial subsidy period and no appropriate measures or targets for patients who are malnourished or underweight. Members considered that, in line with the criteria in place for Standard Supplements, initial Special Authority expiry should be 3 months and follow the criteria for malnutrition and weight loss.

Paediatric products

4.19 The Subcommittee noted that total paediatric product expenditure has grown 29% over the last five years. Members noted that RTD oral feeds make up the bulk of this expenditure and growth, Members also considered that this growth maybe as a result of inappropriate prescribing. Members noted that the current Special Authority criteria are for conditions that would require a referral to the paediatrician and that this would be the most appropriate prescriber to apply for initial funding. Members noted that it would be appropriate to change the wording for the paediatric products to be 'only from a dietitian or paediatrician, or vocational registered general practitioner on the recommendation of a dietitian or paediatrician. Members noted that transitioning some patients from a paediatric product can take up to a year in higher need groups such as Autistic Spectrum Disorder.

4.20 The Subcommittee considered that 'faltering growth' is the term used in Special Food Special Authorities but is not defined in the Pharmaceutical Schedule, members also considered that 'failure to thrive' is also used and defined but not a recommended term. Members considered that 'faltering growth' is the preferred term for insufficient weight gain or inappropriate weight loss. Members **recommended** that all definitions should be reviewed by the Subcommittee, this could be done via email.

Renal products

4.21 The Subcommittee noted that total renal products expenditure has grown steadily over the last five years. Members considered that the definition used for patients to access treatment (acute or chronic kidney disease) is not well defined and likely to encourage inappropriate prescribing. The Subcommittee **recommended** that the criteria should be reworded to 'The patient has acute kidney disease requiring hospitalisation or chronic kidney disease 4 (CKD 4) or more'.

Standard supplements

4.22 The Subcommittee noted that the Standard Supplements Therapeutic Subgroup accounts for 30% of the Special Foods expenditure and has experienced a 16% growth over the last five years. Members noted that RTD oral feeds (1.5 kcal / ml) were reference priced to the oral feed powders in 2011 and whilst this has halved the expenditure in the RTD group of products, oral feed powders growth continues at a significant rate. Members noted that there have been significant issues with continuity of supply of these oral feed powders in New Zealand and considered that reports of exporting may account for part of the reason. Members considered that access inequities arise with additional pharmacy fees are charged on top of the prescription for faxed prescriptions and handling costs, Members noted that this is an issue between pharmacy contracts with wholesalers and their services agreement with DHBs.

4.23 Members considered that there are particular issues in hospitals (who mainly use the RTD formulas for inpatients) and then have to transition patients to powdered oral feeds for community use when they are not subsidised for an indication.

4.24 The Subcommittee considered that the 'food first' principle is not being followed in primary care and education is needed to reinforce this principle. Members considered once a patient commences on Special Foods in the community they are less likely to re-introduce store bought foods back into their diet.

4.25 The Subcommittee considered that there are large amounts of Special Foods that are wasted when patients are commenced on treatment with a particular type of Special Food. Given the cost per tin and usage, Members considered that all initial dispensings should be made for one or two weeks (or a reasonable outer pack size) instead of providing a full month. Members considered this would allow patients to trial the palatability of formulations and flavours; Members noted that this facility was already available via the prescription and pharmacy dispensing software as a 'trial dispensing' and PHARMAC should communicate this with prescribers and pharmacies. The Subcommittee considered that some patients do not reach BMI criteria for malnutrition (for example Non-CF bronchiectasis) and considered that a review of the short and longer term medical conditions for Standard Supplements should be reviewed, Members considered a review of these medical conditions by email could be made prior to consulting on a change.

*2. **Summary of Previous Recommendations/ Action Points***

4.26 The Subcommittee noted a summary of previous recommendations/action points from the Special Foods Subcommittee meetings and a status update on each. Members noted a number of action points that can be deleted as they were no longer relevant or required. (2013 recommendation for NutriniDrink, 2012 recommendation for Polycal and Carb Plus).

5 Correspondence

Supplier application – textured modified foods

5.1 The Subcommittee noted that an application has been made to PHARMAC for the subsidy of texture modified foods to be listed on the Pharmaceutical Schedule. Members considered that on the evidence provided that its previous and current recommendation for food thickeners should apply to this application, that is, food thickeners should not be listed on Section D of the Pharmaceutical Schedule.

5.2 The Subcommittee considered the evidence provided which considered the health economic impact of managing patients following a community-based diagnosis of malnutrition in the UK (Guest et al. Clinical Nutrition. 2011; 30: 422-429). Members considered that the evidence did not consider the benefit of texture modified foods were any different to current treatment options or relevant to the New Zealand clinical setting. The Subcommittee considered it would relook at the application when evidence of benefit relevant to New Zealand was provided.

Carbohydrate Supplement (Polycal) and Fat Modified Feed (Monogen)

5.3 The Subcommittee noted correspondence received on behalf of the Adult and Paediatric National Metabolic Service requesting an extension to the carbohydrate supplement (indications other than cystic fibrosis or renal failure) and fat modified feed Special Authority initial and renewal period to three years.

5.4 The Subcommittee **recommended** that the initial and renewal periods for patients taking carbohydrate supplement or fat modified feeds (indications other than cystic fibrosis or renal failure) should be extended to three years with a high priority. Members considered these patients have long term conditions and are co-prescribed other modular supplements that have three-year expiry. Members did not consider that this would have an impact on expenditure.

5.5 The Subcommittee noted a request to add into the 'fat modified feed' Special Authority a criterion including 'fatty acid oxidation inborn error of metabolism disorder- excluding MCAD deficiency'. Members considered that the current Special Authority criteria of 'metabolic disorders of fat metabolism' adequately covers these patients and considered that current criteria sufficient. Members noted that MCAD deficiency was a contraindication to using this supplement and contraindication are not routinely used in Special Authorities.

5.6 The Subcommittee considered that access to 'fat supplement' via the criterion 'for use in a ketogenic diet' meant that the interpretation of ketogenic diet was not made by a neurologist and could result in use outside of a tightly controlled ketogenic diet such as Atkins diet. Members **recommended** that 'for use in a ketogenic diet' criteria should be removed from this group and made into a new group with criteria currently in place for 'ketogenic diet' which would limit applications in this indication to metabolic physicians and neurologists only.

Danone Nutricia – recognition of AllerPro as an extensively hydrolysed formula

5.7 The Subcommittee noted correspondence from Danone Nutricia requesting that Aptamil Gold+ AllerPro be recognised as an extensively hydrolysed infant formula in respect to the Special Authority criteria for amino acid formula currently in place. Members considered that it would pose a considerable clinical and fiscal risk if the Special Authority referenced a product that is not listed on the Pharmaceutical Schedule, under contract with PHARMAC and has not undergone clinical evaluation for listing on the Pharmaceutical Schedule. Members considered that if Danone Nutricia wished for Aptamil Gold+ AllerPro to be considered as an extensively hydrolysed formula it should provide a funding application for listing on the Pharmaceutical Schedule.

Danone Nutricia – requesting to delist Vitadol C

5.8 The Subcommittee noted correspondence from Danone Nutricia requesting to delist Vitadol C from the Pharmaceutical Schedule. Members noted that Vitadol C is a combination oral liquid which provides 1000 units of vitamin A, 400 units of vitamin D and 30 mg of ascorbic acid per 10 drops, members noted that the ascorbic acid amounts are clinically insignificant and are used to extend the shelf life of the product.

5.9 Members considered that Vitadol C is currently in use for premature babies, paediatric patients with cystic fibrosis, liver disease, fat malabsorption or patients on a very low LCT diet; members considered that having a combination product meant that some patients did not receive enough of one vitamin, or, could potentially receive toxic amounts of the other in order to achieve correct dosing.

5.10 The Subcommittee considered that in the absence of Vitadol C PHARMAC should source separate vitamin A (~1,250 IU per drop/measure strength) and D (~400 IU per drop/measure strength) liquid preparation. Members considered that PHARMAC should consult with neonatologists regarding suitability in preterm infants. Members noted that these patients have a high health need and it is essential that there is a combination product or two with separate vitamins. Members noted that there are no registered products available in New Zealand and PHARMAC may need to consider sufficient time to procure a product and transition hospitals and patients. Members considered that vitamin A and D liquid should be restricted to paediatric patients without further restriction.

6 FruitVits & PhlexyVits for Ketogenic Diet

Application

6.1 The Subcommittee reviewed funding applications from a Canterbury DHB clinician for multivitamin supplements (FruitVits and PhlexyVits) for patients on the ketogenic diet.

Recommendation

6.2 The Subcommittee **recommended** that the funding application for FruitVits and PhlexyVits for patients on ketogenic diet be declined.

Discussion

6.3 The Subcommittee noted that there are 30-40 patients between Canterbury and Auckland DHBs that are managed on ketogenic diets, members noted that national numbers are dependent on DHBs capacity to manage patients. Patient's tube fed KetoCal and those

on Modified Ketogenic Diet therapy would not require a complete multivitamin and mineral supplement.

6.4 Members noted that this application was for paediatric patients with epilepsy on the ketogenic diet, the applicant considers that patients on the ketogenic diet miss out on essential vitamins and minerals as a result of the restricted diet and that these formulations are specifically formulated for patients on restrictive therapeutic diets. Members considered that the most significant long term adverse effects, provided by the applicant, resulting from the ketogenic diet are reduced bone mineralisation (Bergqvist et al. Am J Clin Nutr. 2008; 88:1678-84) and selenium deficiency causing prolonged QT intervals.

6.5 The Subcommittee reviewed additional references provided in the application and considered that most of this evidence related to cost effectiveness and efficacy of the ketogenic diet compared with usual care and did not compare the use of vitamin supplementation in the ketogenic diet.

6.6 Members noted that patients historically initiated onto a ketogenic diet in hospital, a multivitamin preparation had been prescribed (Ketovite liquid and tablets, cost of ~60 cents per day). Members noted that this supplement had been delisted in September 2010 due to low sales and the cost of registration. The applicant considers that currently available multivitamin and mineral preparations (both over the counter and subsidised) are not suitable due to having high levels of carbohydrate which means patients are likely to exceed their carbohydrate allowance that could be around 10 g per day. Members considered it is unclear how many patients are unable to stay on the Ketogenic Diet due to the unsuitability of available multivitamins.

6.7 The Subcommittee considered that the evidence for use of a particular supplement is poor noting that it is not clear what the nutrient requirements are. Members considered that the likely comparator for these patients is calcium, vitamin D and selenium supplementation. Members noted that the evidence provided is primarily consensus statements based on recommendations of the international Ketogenic Study group (Kossoff EH, et al. Epilepsia. 2009; 50(2): 304-317) and the International League Against Epilepsy Task Force for Dietary Therapy (Kossoff et al. Epilepsia. 2015; 56(9):1337–1342) which considered there was evidence for the use of a multivitamin (including Calcium and vitamin D) with trace elements (including selenium) and that there should be a preference for carbohydrate free or low carbohydrate formulations. If a carbohydrate containing formulation was used it should be included in the dietary allowance calculations. A specific formulation has not been studied or recommended.

6.8 The Subcommittee consider that the application proposed a high cost (~$10 per day) compared with currently funded multivitamin preparations or for those that are not funded but available over the counter. It is unclear what, if any, benefit would be provided by the proposed supplement over these alternatives. The Subcommittee consider that the evidence for use of a complete multivitamins with trace elements product in patients on the Ketogenic Diet is theoretical and guidance is based on consensus statements.

7 Enteral Feeds (Nutrini Peptisorb and Peptisorb Energy)

Application

7.1 The Subcommittee reviewed a funding application from a supplier to consider Nutrini Peptisorb and Nutrini Peptisorb Energy for paediatric patients with impaired gastrointestinal function who do not tolerate polymeric feeds or for whom polymeric feeds are not suitable.

Recommendation

7.2 The Subcommittee **recommended** that Nutrini Peptisorb and Nutrini Peptisorb Energy be listed on the Pharmaceutical Schedule with a high priority for paediatric patients with impaired gastrointestinal function who do not tolerate polymeric feeds or for whom polymeric feeds are not suitable.

Discussion

7.3 The Subcommittee noted that Nutrini Peptisorb/Nutrini Peptisorb Energy are ready to hang, semi elemental formulas that are nutritionally complete and are intended for tube feeding. Both have extensively hydrolysed whey protein with a 50:50 ratio of medium chain triglycerides to long chain triglycerides. Nutrini Peptisorb is 1 kcal / ml and intended for patients 1-6 years of age or 8-20 kg, Nutrini Peptisorb Energy is 1.5 kcal / ml and intended for patients 1-14 years of age or 8-45 kg.

7.4 The Subcommittee noted that for paediatric patients who currently require a semi-elemental formula to be delivered via the enteral route, staff do so by reconstituting powdered infant formula. Consequently there are additional costs of consumables such as bottles and bungs for administration of the mixed formula, labour time for mixing and a reduced hang time from 24 to 4 hours as opposed to pre-formulated feeds. Infant formulas do not meet the micronutrient requirements of children over 2 years of age. The Subcommittee considered that mixing these formulae adds a risk that a mistake is made in the concentration which may have a negative health impact on the patient.

7.5 The Subcommittee considered that there would likely be 10 patients across New Zealand who would access these products and listing would likely be a minimum of cost neutral to the health section when alternatives, time and consumables are taken into consideration. The Subcommittee noted that these are vulnerable patients with intestinal failure from a variety of causes, such as extensive small bowel mucosal disease and short bowel syndrome.

7.6 The Subcommittee considered that the Nutirini Peptisorb/Nutrini Peptisorb Energy is a food for special medical purpose and is an acceptable formulation to be included in Section D and part II of Section H of the Pharmaceutical Schedule under the Gastrointestinal and Other Malabsorptive Problems Therapeutic Subheading of the Infant Formula Group. Members considered that it would be appropriate to use the same criteria that exists for extensively hydrolysed infant formula.

8 Infant Formula

8.1 PHARMAC received three funding applications for new or replacement infant formula products to be considered by the Special Foods Subcommittee. Members considered that these applications were for formulations to be included on the Pharmaceutical Schedule under the amino acid and extensively hydrolysed Therapeutic Subgroup.

8.2 The Subcommittee considered that a commonly used way to describe elemental infant formula was to refer to the Dalton size, Members noted that a Dalton measure described the protein size in the infant formula. Members considered that an extensively hydrolysed infant formula should have 95% of proteins less than 1000 Daltons. The Subcommittee considered that the currently available extensively hydrolysed formula does not meet this requirement.

8.3 Members noted that amino acid formula is currently overused in New Zealand and considered that it would be possible to run a competitive process for infant formula. Members considered there was a clinical preference to have more than one extensively hydrolysed and amino acid infant formula available for taste and composition reasons.

Neocate Syneo

Application

8.4 The Subcommittee reviewed a funding application from a supplier to review the funding of Neocate Syneo in replacement of Neocate LCP, a special food for infants with a cow milk protein allergy (CMPA) and multiple food protein intolerance (MFPI), eosinophilic oesophagitis and for severe intolerance or malabsorption.

Recommendation

8.5 The Subcommittee **recommended** that Neocate Syneo was an acceptable replacement for Neocate LCP, members considered that it should be cost neutral to Neocate LCP or Neocate Gold.

Discussion

8.6 The Subcommittee noted that Neocate Syneo is a nutritionally complete amino acid synthetic formula supplemented with long chain polyunsaturated fatty acids, medium chain triglycerides, synbiotics (prebiotics and probiotics) and nucleotides. Members noted that this formulation's difference was that it contained a prebiotic and probiotic blend and a higher proportion of medium chain triglycerides (MCTs).

8.7 The Subcommittee noted that a significant number of references were provided in the application and the applicant considered the following to be of most support to the application:

- Harvey et al. Pediatric Research. 2014; 75(2): 343-351.
- Burks et al. Pediatric Allergy and Immunology 2015; 26: 316-322.
- Michaelis et al. 2016 – *EACCI abstract - presented June 2016*

The Subcommittee did not consider that from the evidence provided that the addition of prebiotics and probiotics provided any proven health gains above the existing amino acid formula currently available. The Subcommittee considered that the addition of higher MCT may be beneficial in babies with long chain fat malabsorption.

The Subcommittee considered that having an amino acid formula listed on the schedule that has less than or equal to 30% MCT was important for patients where high MCT is contraindicated. Members also considered it is similarly important to have an amino acid formula without pre or probiotics.

8.8 The Subcommittee considered that formulation of Neocate Syneo was similar to that of Neocate LCP and it would be an appropriate replacement.

Alfamino

Application

8.9 The Subcommittee reviewed a funding application from a supplier to consider the addition of Alfamino as an amino acid infant formula.

Recommendation

8.10 The Subcommittee **recommended** that Alfamino be listed as an amino acid formula on the Pharmaceutical Schedule with a high priority. The Subcommittee considered that such a listing should be cost neutral or cost saving to the combined pharmaceutical budget.

Discussion

8.11 The Subcommittee noted that Alfamino is an amino acid formula which has similar macronutrients as currently available amino acid infant formulae. Alfamino is an amino acid formula, standard dilution provides 0.68 kcal/ml, with similar MCT as Neocate Gold and is formulated for use from birth to 12 months of age. Members noted that Alfamino was considered by the PBAC as a minor submission and is currently listed on the PBS.

8.12 The Subcommittee noted that Alfamino is considered hypoallergenic by definition of the American Academy of Paediatrics definition in a randomised, double blind, cross over study (Nowak-Wegrzyn A, et al. Clin Pediatr 2015; 54(3): 264–72) which compared Alfamino to Neocate Gold. Members considered that Alfamino is hypoallergenic and non-inferior to Neocate Gold.

8.13 Members considered that it would be clinically appropriate for patients taking other amino acid formula to switch to Alfamino if required and that they would not require additional clinical input. Members noted that some patients may prefer the taste of one formula over another and that taste preference occurs in all oral nutritional supplements to a degree.

8.14 The Subcommittee consider it possible that if listed, the amino acid Therapeutic Subgroup could be reference priced to Alfamino based on kcal per 100 ml at standard dilution, if it were a lower price that currently listed amino acid formula. Members considered that it would be possible to have only one supplier of amino acid formula if there were guarantees put in place that secured supply. Members considered that it would be preferable for there to be two for taste alternatives.

8.15 The Subcommittee did not consider that listing of Alfamino would cause any additional expenditure, members considered that this would not increase patient numbers or usage. Members also considered that it would likely reduce expenditure due to the lower price.

Pepticate

Application

8.16 The Subcommittee reviewed a funding application from a supplier to consider Pepticate to be listed as an additional extensively hydrolysed infant formula in Section D and Part II of Section H of the Pharmaceutical Schedule.

Recommendation

8.17 The Subcommittee **recommended** that Pepticate be listed on the Pharmaceutical Schedule if cost neutral to Aptamil Gold+ Pepti Junior to allow access for an alternative extensively hydrolysed infant formula.

Discussion

8.18 The Subcommittee considered that Pepticate meets the American Academy of Paediatrics definition for hypoallergenic and is endorsed by the European Society of Paediatric Gastroenterology (ESPGAN- Giampietro et al. Pediatric Allergy and Immunology. 2001; 12.2:83-6). Members noted that Pepticate is a 0.67 kcal / ml, nutritionally complete extensively hydrolysed infant formula.

8.19 The Subcommittee noted that peptide comparison between Pepticate had a lower proportion of peptides greater than 1500 Daltons compared with Aptamil Gold+ Pepti Junior. Members noted that the percentage of fat from Medium Chain Triglycerides was less in Pepticate (15%) compared with Aptamil Gold+ Pepti Junior (50%). Members noted that Pepticate contains lactose. Members considered that the Dalton size and MCT characteristics meant that this product was suitable for allergy but not an ideal product for gastrointestinal intolerance. Therefore it could not be used as a substitute for Aptamil Gold+ Pepti Junior.

8.20 The Subcommittee considered that Pepticate may be better tolerated than Aptamil Gold+ Pepti Junior for patients with cows milk allergy needing an extensively hydrolysed formula. Members considered that it may not be appropriate for patients with LCT malabsorption.

9 AdVital

Application

9.1 The Subcommittee reviewed a funding application from a supplier to consider the funding of AdVital for the treatment of malnutrition in adults.

Recommendation

9.2 The Subcommittee **recommended** that AdVital be listed as an oral feed powder on the Pharmaceutical Schedule with a medium priority for patients who meet the Standard Supplements Special Authority and who have taste fatigue.

9.3 The Subcommittee **recommended** that AdVital be listed as an oral feed powder on the Pharmaceutical Schedule under the Standard Supplements Special Authority if cost neutral to currently funded oral feed powders.

Discussion

9.4 The Subcommittee noted that Advital is a nutritionally complete oral powdered feed that at one scoop provides 0.8 kcal / ml when mixed with 200 ml of water. Members noted that Advital has a neutral flavour which means that is can be added to range of food or drinks.

9.5 The Subcommittee noted that Advital by weight has an equivalent number of calories and amount of carbohydrate, a higher level of protein, lower level of fat and sugar than currently funded oral feed powders. Members noted that the osmolarity was lower than currently funded alternatives which may make it more tolerable for patients post bowel surgery or similar medical circumstances.

9.6 The Subcommittee reviewed the following evidence provided by the applicant.

- Agarwal et al. Nutrition & Dietetic. 2015; 72: 69–73.
- Agarwal et al. Clinical Nutrition. 2013; 32(5): 737-45.
- Moynihan et al. Public Health Nutrition. 2004; 7(1A): 201–226.
- Parrish et al. Practical Gastroenterology. 2005; 9: 67-106.

9.7 The Subcommittee noted that malnutrition has a large impact on the health system and considered that malnutrition can increase hospital length of stay, readmission rates and mortality. Members considered that the evidence provided demonstrated this effect. However there was not specific evidence that demonstrated that Advital provided a benefit over and above what is currently funded on the Pharmaceutical Schedule. Members noted that Advital was more expensive than currently available oral feed powders and without additional proven benefit it would be difficult to justify paying a premium for.

9.8 The Subcommittee considered that there are benefits to Advital in that it requires one scoop per serve and that it is tasteless. This provides suitability benefits to patients remembering the correct number of scoops to use and those patients that struggle with taste fatigue. The Subcommittee considered that would be difficult to limit the use of Advital to the patient group who would get the most health benefit from this formulation and, given the cost of Advital, listing it alongside existing formulations of oral feed powders would pose a budget risk. Members considered targeting treatment with a Special Authority developed for ‘taste fatigue’ would be the patient group that would benefit most from this formulation and consider that one could be developed via email with the Special Foods Subcommittee, noting that it would be difficult to define a patient with ‘taste fatigue’ separately to those that have a flavour preference.

10 Cubitan

Background

10.1 The Subcommittee reviewed a second funding application from a supplier to review the widening of access of Cubitan, a nutritional supplement to aid in the recovery of pressure ulcers (PU).

10.2 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.

Recommendation

10.3 The Subcommittee **recommended** that the revised funding application for Cubitan to aid in the recovery of pressure ulcers be declined.

Discussion

10.4 The Subcommittee noted a review made by the Dermatology Subcommittee at its December 2017 meeting of Cubitan and the resubmitted evidence requested. Members noted that the Dermatology Subcommittee recommended that the application be declined and 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.

10.5 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.

10.6 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.

- The Subcommittee agreed with the Dermatology Subcommittee assessment of the trial and considered that the exclusion criteria for the study removed many patients in New Zealand who would experience pressure ulcers.

10.7 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(1):246-52).

- The Subcommittee agreed with the Dermatology Subcommittee evaluation and considered that the evidence was of low quality and modest benefit. Members considered that it would be challenging to apply this to the New Zealand setting.

10.8 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.

- The Subcommittee agreed with the Dermatology Subcommittee evaluation and considered that the findings would need to be supported by large sample RCTs with consistent outcomes and reporting.

10.9 The Subcommittee considered that Arginine is widespread in food and in line with a ‘food first’ approach considered that good nutrition heals pressure ulcers. Members considered that there is no evidence provided that indicates that Cubitan or arginine rich foods are any better at healing pressure ulcers than good nutrition.