Special Foods Subcommittee of PTAC meeting

held 21 November 2008

(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 2008*:

Note that this document is not necessarily a complete record of the Special Foods Subcommittee meeting; only the Minutes relating to Special Foods Subcommittee discussions about an application that contains a recommendation in relation to an application are 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.

Some material has been withheld form the Minute in accordance with the following withholding grounds in the Official Information Act 1982 (OIA) to:

- protect the privacy of natural persons (section 9(2)(a))
- enable a Minister of the Crown or any department or organisation holding the information to carry on, without prejudice or disadvantage, negotiations (including commercial and industrial negotiations (section 9(2)(j))

Contents

1 Elemental Formula

1.1 The Subcommittee considered an application from Abbott for the listing of EleCare in the Pharmaceutical Schedule, an application from Nutrica for adding LCP's (long-chain phospholipids) to Pepti Junior and a proposal to amend the Special Authority for elemental formula.

EleCare

1.2 The Subcommittee noted that EleCare is a totally hydrolysed elemental formula for use in the dietary management of children with severe cow's milk allergy and multiple food protein intolerance or other indications requiring an elemental diet, when the patients can not tolerate peptide-based formulas.

1.3 The Subcommittee noted that international guidelines recommend that patients with cow's milk allergy, who are under 6 months, should not use soy based formulas and that even up to 2 years of age soy formula should be carefully considered before being used.

1.4 The Subcommittee noted that currently listed alternative products include Neocate, Neocate Advance, and Vivonex Pediatric, although it was noted that Vivonex Pediatric can only be used for children over one year of age.

1.5 The Subcommittee noted that EleCare could be used by a wider range of ages than Neocate as a child changes from the Neocate brand to the Neocate Advance brand at one year of age.

1.6 The Subcommittee considered the application from Abbott was of good quality although members noted that the level of Vitamin D in the submission on page 10 is wrong.

1.7 The Subcommittee accepted that the previous concerns regarding the vitamin A level being too high and the discrepancy between the amount of Vitamin A shown on the product labelling and in the original submission had been explained by the supplier. The Subcommittee noted that the formulation had been adjusted to reflect the Food Standards of Australia and New Zealand and that the amount of Vitamin A in EleCare is similar to the amount in Neocate and Neocate Advance. The Subcommittee considered that there is a risk that the Vitamin A level was too high if EleCare or Neocate Advance is used as a complete source of nutrition for babies over 12 months of age. The Subcommittee therefore considered that the Special Authority Form should state the maximal concentration and maximal amount that should be used and requested that PHARMAC staff discuss developing appropriate guidelines with the Paediatric Dietician's Special Interest Group of NZDA.

1.8 The Subcommittee considered that an advantage of EleCare over Neocate and Neocate Advance was that a change in product was not needed as the child aged.

1.9 The Subcommittee considered that EleCare has the same or similar clinical effect to Neocate and Neocate Advance and that these products should be included in the same reference price group. The Subcommittee considered that as these products had a similar clinical effect and that reference pricing was appropriate.

1.10 The Subcommittee **recommended** that EleCare be listed in the Pharmaceutical Schedule if cost neutral compared to currently listed elemental formulas – Vivonex Pediatric and both presentations of Neocate.

2 PKU Products

2.1 The Subcommittee considered applications for, the listing of Add-Ins (Nutricia), the listing of PKU Cooler System (Vitaflo) and the listing of PKU Gel (Vitaflo) for the management of phenylketonuria (PKU).

Add-Ins

2.2 The Subcommittee noted that Add-Ins is a protein substitute that contains free amino acids, excluding phenylalanine and micronutrients encapsulated in a fat coating which masks the unpleasant taste and smell of amino acids. The Subcommittee also noted that Add-Ins is to be sprinkled over warm or cold food and can be used from 4 years of age, and that it also contains vitamins.

2.3 The Subcommittee noted that the price of Add-Ins would be $[withheld under section 9(2)(j) of the OIA] per gram of protein which is the same as the most expensive currently listed PKU supplement, Easiphen.

2.4 The Subcommittee noted the inclusion by the supplier of a local evaluation of Add-Ins [withheld under section 9(2)(a) of the OIA] and a letter from [s9(2)(a)] supporting the application. The Subcommittee noted that in the local evaluation, ten outpatients were provided with some food items and Add-ins and asked to rank the products according to appearance, taste and smell. Seven of the patients preferred Add-Ins to their current protein substitute.

2.5 The Subcommittee considered that children would start with a PKU product such as XP Analog LCP but would then switch to XP Maxamaid and then XP Maximum, and that [withheld under section 9(2)(a) of the OIA] compared Add-ins with XP Maxamaid and then XP Maximum. The Subcommittee also considered that Add-Ins are likely to be used in combination with Easiphen

PKU Cooler System

2.6 The Subcommittee noted that the PKU Cooler System is a low volume ready to drink protein substitutes to be used from the age of 3. The Subcommittee noted that there are 3 different pack sizes (87 ml, 130 ml and 174 ml) and the concentration of the solution is the same in all pack sizes.

2.7 The Subcommittee considered that the packets were convenient and practical especially for older children, that the different pack sizes could decrease wastage, and that nutrients contained in the PKU Cooler System were sufficient.

2.8 The Subcommittee noted that the price of PKU Cooler system would be lower than currently listed comparable products and that even though the packs were trendy for the adolescent market overuse would not occur due to the taste of the product.

PKU Gel

2.9 The Subcommittee considered the application for PKU Gel, which is a powder which when mixed with water forms a gel. The Subcommittee noted that it can be used from 6 months of age, and that it contains carbohydrates, vitamins, minerals and trace elements in levels appropriate to meet the New Zealand Nutrient Reference Values.

2.10 The Subcommittee considered that for babies over 6 months old the comparator to PKU Gel would be XP Analog LCP. The Subcommittee also considered advantages of PKU Gel included it being a low volume product, its taste, it being an alternative for babies over 6 months, and it being administered by a mouth syringe.

Metabolic Unit Consultation

2.11 The Subcommittee noted that while Add-Ins, PKU Cooler System and PKU Gel appeared to be good products there may be a number of other attractive products available. The Subcommittee therefore recommended that PHARMAC staff consult with the National Metabolic Service to determined appropriate products.

Recommendation

2.12 The Subcommittee considered that reference pricing of Add-Ins, PKU Cooler System and PKU Gel and the current PKU products could occur based on protein content.

2.13 The Subcommittee **recommended** that Add-Ins, PKU Cooler System and PKU Gel be listed on the Pharmaceutical Schedule with a high priority, provided that this recommendation is agreed to by the National Metabolic Service.

3 TYR Cooler

3.1 The Subcommittee considered an application for TYR Cooler, a ready to drink liquid, for the management of tyrosinemia in children over 3 years of age, adolescents and adults. The Subcommittee noted that there are currently no products listed in the Pharmaceutical Schedule for the treatment of this disease.

3.2 The Subcommittee noted that this product can only be used for patients over 3 years of age, and considered that information from the supplier should be obtained as to whether there is another product for younger children available.

3.3 The Subcommittee noted that the proposed price for TYR Cooler of $[withheld under section 9(2)(j) of the OIA] is the same price per gram of protein as the proposed price on MSUD Express Cooler.

3.4 The Subcommittee noted that there are only 1-2 patients in New Zealand suffering from this disease and therefore patients with the disease could be evaluated under Exceptional Circumstances (EC). However the Subcommittee considered that a listing could be favourable as it would reduce administration for prescribers and the EC panel as well as ensuring stock availability. The Subcommittee considered that PHARMAC staff should consult the EC panel.

3.5 The Subcommittee considered that PHARMAC staff should ask this and other suppliers about other products for this indication, including the powders, as well as consult with the National Metabolic Service as to which products are desirable.

3.6 The Subcommittee **recommended** that TYR Cooler be listed on the Pharmaceutical Schedule with a high priority, subject to an assessment of the product by the National Metabolic Service.

4 MSUD Express Cooler

4.1 The Subcommittee considered an application for MSUD Express Cooler, a ready to drink low-volume liquid, for the management of maple syrup disease in children from 3 years of age, adolescents and adults. The Subcommittee noted that there are currently two powder products, Maxamum and Maxamaid, listed in the Pharmaceutical Schedule for the treatment of this disease.

4.2 The Subcommittee noted that the proposed price of $[withheld under section 9(2)(j) of the OIA] per gram of protein is cheaper than the currently listed products, and the cost of a liver transplant which can occur as a result of disease progression.

4.3 The subcommittee considered that the product is convenient to use as it does not need to be mixed up and this and its better taste may increase compliance.

4.4 The Subcommittee noted that there are only 1-2 patients in New Zealand suffering from this disease and therefore patients with the disease could be evaluated under Exceptional Circumstances (EC). However the Subcommittee considered that a listing could be favourable as it would reduce administration for prescribers and the EC panel as well as ensuring stock availability. The Subcommittee considered that PHARMAC staff should consult the EC panel.

4.5 The Subcommittee **recommended** that MSUD Express Cooler be listed on the Pharmaceutical Schedule with a high priority, subject to an assessment of the product by the National Metabolic Service.

5 HCU Cooler

5.1 The Subcommittee considered an application for HCU Cooler, a ready to drink low-volume liquid, for the management of homocystinuria in children over 3 years of age, adolescents and adults. The Subcommittee noted that there is currently only one product XMET Maxamum, which is a powder, listed for the treatment of this disease.

5.2 The Subcommittee noted that this product can only be used for patients over 3 years of age, and considered that information from the supplier should be obtained as to whether there is another product for younger children available.

5.3 The Subcommittee noted that the price of the product is proposed to be $[withheld under section 9(2)(j) of the OIA] per gram of protein which is cheaper than the currently listed product.

5.4 The Subcommittee considered that the product is convenient to use as it does not need to be mixed up and this and its better taste may increase compliance.

5.5 The Subcommittee noted that there are only 1-2 patients in New Zealand suffering from this disease and therefore patients with the disease could be evaluated under Exceptional Circumstances (EC). However the Subcommittee considered that a listing could be favourable as it would reduce administration for prescribers and the EC panel as well as ensuring stock availability. The Subcommittee considered that PHARMAC staff should consult the EC panel.

5.6 The Subcommittee **recommended** that HCU Cooler be listed on the Pharmaceutical Schedule with a high priority, subject to an assessment of the product by the National Metabolic Service.

6 Modulen IBD

6.1 The Subcommittee considered an application for the listing of Modulen IBD for the treatment of Crohn's disease. The Subcommittee noted that the total number of patients with Crohn's disease in New Zealand is estimated to be between 6,000 and 8,000 and that there are a variety of medical and surgical treatments available for Crohn's disease. The Subcommittee noted that Modulen IBD is a nutritionally complete milk based drink for oral or tube-feeding use, that it can be used as a complete diet for 6-8 weeks or as a supplement, and that it contains anti-inflammatory transforming growth factor (TGF-β).

6.2 The Subcommittee noted two studies included in the application that investigated the use of Modulen IBD in children with Crohn's disease. The Subcommittee noted that a study in 2000 by Fell et al (Aliment Pharmacol Ther 2000; 14:281-289) which reported 29 children with active Crohn's disease going into complete remission after consuming Modulen IBD as a sole source of nutrition for 8 weeks, and that 60% of these children did not experience relapse during ten months of follow up as well as having a median weight gain of 3.2 kg. The Subcommittee noted another study by Borelli et al (Clinical Gastroenterology and Hepathology 2006: 4 (6): 1-10) which randomised children to either Modulen IBD or oral corticosteroids for ten weeks and found that the proportion of children who achieved remission was comparable between the two groups, however mucosal healing was significantly higher in the Modulen IBD group.

6.3 The Subcommittee noted an additional study by (Hartman C et al, 2008: IMAJ; 10, 503-507) which evaluated 28 children and adolescents (median age 14 years) suffering from Crohn's disease retrospectively after receiving Modulen IBD as a nutritional supplement to their regular diet in addition to appropriate medical therapy. The Subcommittee noted that the patients were compared to a historical group of patients, matched for age and disease severity, who were supplemented with conventional formula (Ensure Plus), and also with patients who received drug treatment as their sole therapy. The Subcommittee noted that the clinical manifestations, growth and the Pediatric Crohn's Disease Activity Index (PCDAI) were recorded. The Subcommittee noted that of 28 children only one third used Modulen IBD (the others did not use it due to a variety of factors including low palatalability, high cost or lack of motivation) and that these children and the children using Ensure Plus, but not the non-supplemented group, showed a significant decrease in PCDAI. The Subcommittee also noted that; only in the Modulen IBD group were significant improvements in body mass index and erythrocyte sedimentation rate recorded at follow-up (median 3.4 months), that significantly fewer children had severe disease in the Modulen IBD group at follow-up; and that significantly more children achieved and attained remission in the Modulen IBD group. The Subcommittee did however note that some of the children initiated drug therapy during this time, and therefore it is uncertain how much of the response could be attributed to the nutritional support or the drug-therapy.

6.4 The Subcommittee considered that while enteral therapies have been demonstrated to induce remission in children and adolescents, the data in adults is inconclusive.

6.5 The Subcommittee also considered that enteral therapy is more appropriate in children as steroids can impair growth. The Subcommittee therefore considered that nutrition was a valuable, but currently underused, treatment method for paediatric patients and that if Modulen IBD was available then it would be used.

6.6 The Subcommittee considered that for adult patients the use of Modulen IBD would be as a supplement, that it may be overused, and that the evidence was not as good.

6.7 The Subcommittee considered that advantages of Modulen IBD included that it could be used orally, and that it was more palatable than the alternative of naso-gastric enteral feeding, and that it has an additional benefit due to TGF-β.

6.8 The Subcommittee considered that additional information should be provided as the studies are small and are not blind. The Subcommittee also considered that the patient numbers were underestimated and the cost of treatment with prednisone was overestimated.

6.9 The Subcommittee **recommended** that an opinion on the application and potential guidelines for use in the paediatric population should be obtained from some paediatricians. The Subcommittee **recommended** that listing Modulen IBD should not be considered for adults due to insufficient evidence although this could be reconsidered if more evidence became available.

7 Multivitamins and minerals for Ketogenic Diet

7.1 The Subcommittee noted an application to widen access to multivitamin supplements and minerals (specifically Ketovite tablets, Ketovite Liquid and Metabolic Mineral Mixture) to include children on a Ketogenic diet to treat epilepsy. The Subcommittee noted that the application was discussed by PTAC at its February 2008 meeting and that PTAC recommended widen access subject to agreement by the Special foods Subcommittee.

7.2 The Subcommittee noted that PTAC had raised questions regarding the importance of adding vitamins and minerals to a ketogenic diet. The Subcommittee considered results from a PHARMAC literature search which indicated that:

- The nutrient intake of vitamins and minerals were lower for children with intractable epilepsy as compared to healthy children and vitamin/mineral supplementation should be considered (Volpe SL et al).
- Multivitamin and mineral supplements are given to all patients on Ketogenic diet at the John Hopkins Medical Institution (the world experts on Ketogenic diet) as the diet is not nutritionally complete (Hartman AL and Vining EPG).
- Selenium deficiency may be a rare complication of the Ketogenic diet (Bergqvist AGC et al).

7.3 The Subcommittee considered that the economic impact of the proposal is low and that it may be cost-savings if the patient is controlled without anti-epileptic products.

7.4 The Subcommittee **recommended** that Ketovite tablets, Ketovite Liquid and the Metabolic Mineral Mix should be subsidised with a high priority for children on a Ketogenic diet in the treatment of epilepsy. The Subcommittee also considered that patients should also use a selenium supplement, such as Selenite drops 150 µg/dr, and that the selenium supplement would not need to be subsidised.

8 Food thickeners

8.1 The Subcommittee considered a proposal from [withheld under section 9(2)(a) of the OIA] DHB regarding widening of access to food thickeners to include any neurological disorder causing dysphagia.

8.2 The Subcommittee noted that widening of access to food thickeners was discussed at the October 2007 meeting and that it was recommended to widen access to include dysphagia as diagnosed by a defined swallowing assessment which could be conducted by a speech-language therapist. In addition it was noted that while expenditure on Food Thickeners was controlled at an annual cost of $3,000 per patient any future widening of access would need to be carefully considered.

8.3 The Subcommittee considered that the current Special Authority criteria did not provide consistent access for similar patient groups and that access should be based on the severity of the swallowing disorder rather than on the disease state.

8.4 The Subcommittee noted that other options for patients included using cornstarch and food as thickeners and other products such as smoothies and milkshakes.

8.5 The Subcommittee considered that there is a risk of overuse and an associated expenditure risk in any widening of access which should be considered.

8.6 The Subcommittee **recommended** that PHARMAC staff consult with speech language therapists, neurologists, dieticians, paediatricians and geriatricians regarding altering the wording of the Special Authority and creating usage guidelines so that food thickeners can be targeted to patient groups which are at most risk.