Record of the Special Foods Advisory Committee Meeting held on 27 October 2023

Special Foods Advisory Committee records are published in accordance with the Terms of Reference for the Specialist Advisory Committees 2021.

Note that this document is not necessarily a complete record of the Special Foods Advisory Committee meeting; only the relevant portions of the meeting record relating to Special Foods Advisory Committee discussions about an application or Pharmac staff proposal that contain a recommendation are generally published.

The Special Foods Advisory Committee 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.

Pharmac Advisory Committees make recommendations, including priority, within their therapeutic groups of interest.

The record of this Advisory Committee meeting will be reviewed by PTAC at an upcoming meeting.

Specialist Advisory Committees and PTAC may differ in the advice they provide to Pharmac, including recommendations' priority, due to the committees' different, if complementary, roles, expertise, experience, and perspectives.

Pharmac is not bound to follow the recommendations made below. Applications are prioritised by Pharmac against other funding options and progressed accordingly. The relative priority of any one funding choice is dependent on a number of factors, including (but not limited to) the recommendation of PTAC and/or Specialist Advisory Committees, the mix of other applications being assessed, the amount of funding available, the success of commercial negotiations and/or the availability of clinical data.

1. Table of Contents

1. Attendance

Present
Chair – Stephen Munn
Alan Fraser
Amin Roberts
Chris Pihema
Jocy Wood
Kim Herbison
Nicky McCarthy
Nicola Hartley
Russell Walmsley
Victoria Woollett

Apologies
Jennifer Martin

2. Summary of recommendations

Pharmaceutical and Indication	Recommendation
• Renilon 4.0 for the nutritional management of children with chronic kidney disease within the context of treatment with special food subject to Special Authority criteria	High priority
• Renilon 4.0 for the nutritional management of adults with chronic kidney disease within the context of treatment with special food subject to Special Authority criteria	Medium priority
• Phlexy-Vits and FruitiVits for ketogenic diet in the setting of epilepsy treatment, and inherited metabolic diseases within the context of treatment with special foods, subject to Special Authority criteria	High priority
• Oral feed 1.5 kcal/mL for exclusive enteral nutrition (EEN) for the treatment of Crohn's disease (CD) in adults within the context of treatment with special foods, subject to endorsement	High priority
• Oral feed 1.5kcal/mL for COPD with hypercapnia current access criteria be	High priority

amended within the context of treatment with special foods	
• Fortisip Compact Protein for currently funded standard supplements indications	High Priority
• KetoCal 4:1 liquid for intractable epilepsy, pyruvate dehydrogenase deficiency or glucose transported type-1 deficiency and other conditions requiring a ketogenic diet	Low priority

3. The role of Specialist Advisory Committees and records of meetings

3.1. This meeting record of the Special Foods Advisory Committee is published in accordance with the Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) 2021 and Specialist Advisory Committees 2021.Terms of Reference describe, *inter alia*, the establishment, activities, considerations, advice, and the publication of such advice of Specialist Advisory Committees and PTAC.

3.2. Conflicts of Interest are described and managed in accordance with section 6.4 of the SAC Terms of Reference.

3.3. The Special Foods Advisory Committee is a Specialist Advisory Committee of Pharmac. The Special Foods Advisory Committee and PTAC and other Specialist Advisory Committees have complementary roles, expertise, experience, and perspectives. The Special Foods Advisory Committee and other Specialist Advisory Committees may therefore, at times, make recommendations for treatments for special foods that differ from PTAC's, including the priority assigned to recommendations, when considering the same evidence. Likewise, PTAC may, at times, make recommendations for treatments for special foods that differ from the Special Foods Advisory Committee's, or Specialist Advisory Committees may make recommendations that differ from other Specialist Advisory Committees'.

Pharmac considers the recommendations provided by both the Special Foods Advisory Committee and PTAC and any other relevant Specialist Advisory Committees when assessing applications for treatments for special foods.

4. Welcome and introduction

4.1. The Chair opened the meeting with a karakia (prayer) and mihimihi (acknowledgements). Then there was a round of whanaungatanga (introductions and relationship building). The Chair welcomed the Committee.

5. Previous action points/recommendations

5.1. The Committee considered the summary of previous recommendations and action points from previous meetings and noted the following.

5.1.1. The Committee noted that a number of previous action points related to the sourcing of new Special Foods items which had since been resolved through Pharmac's close out project. The Committee noted that the majority of these items had been closed as no product was available. The Committee noted however, that new applications for these products could be submitted at any time and would be reconsidered for funding.

5.1.2. The Committee noted a number of open action items were for various Flavour Creations supplements. The Committee considered that these individual actions could be closed and replaced with a new action for Pharmac to engage with this supplier about its range of treatments and its interest in supplying the New Zealand market.

5.1.3. The Committee noted the use of the term 'failure to thrive' within Special Authority criteria and Hospital restriction criteria in the Special Foods Therapeutic Group had been replaced with the term 'faltering growth' in line with previous recommendations from the Special Foods Subcommittee. The Committee considered that this item could be removed from Pharmac's list of actions.

5.1.4. The Committee noted the use of the terms 'acute or chronic renal disease' within the current Special Authority criteria for renal products SA1101 and RS1228 should be updated to specify that the person has been hospitalised with acute kidney disease or has chronic kidney disease stage 4 or 5. Members considered that in some instances the current criteria may be being used to provide a fully funded supplement to people who did not necessarily need it. Amending the criteria should result in more appropriate use of these supplements and reduced expenditure. The Committee considered that a renal specialist would not be required to categorise kidney disease and the proposed changes to the criteria would not create barriers to access.

5.1.5. The Committee reconfirmed the 2017 recommendation from the Special Foods Subcommittee that the initial and renewal periods for people taking carbohydrate supplement or fat modified feeds (for reasons other than cystic fibrosis or renal failure) should be extended to three years. Members did not consider this change would result in additional use of these supplements.

5.1.6. The Committee considered the 2015 recommendation from the Special Foods Subcommittee regarding nutrient modules that the separator prior to the last criterion (for use as a component in a modular formula) for be changed from 'or' to 'and' in Section D of the Pharmaceutical Schedule and remain as 'or' in the hospital medicines list. Members considered that this had been proposed in 2015 as a result of practice at the time where nutrient modules, particularly fat supplements were used in large volumes to provide additional calories. Members noted that this practice was no longer common, and the Committee considered that this change was no longer required and could be removed from the action list.

5.1.7. The Committee noted that the 2015 application for the (full) funding of oral nutritional supplements for people with head and neck cancer had received a medium priority from both the Special Foods Subcommittee and PTAC and was ranked on Pharmac's Options for Investment List but was not currently in a position where funding could be progressed.

5.1.8. The Committee noted that people with head and neck cancer and people with cystic fibrosis 10 years and over were currently able to access fully funded oral feed powder 1kcal/ml. Members discussed that for people with Cystic Fibrosis the effort to mix oral feed powder with liquid could make the task difficult and support from whānau or carers may be required. For people with head and neck cancer it was noted that the texture of oral feed powder, which tended to be more gritty than liquid options, could be difficult to swallow for individuals undergoing treatment or recovering from surgery.

5.1.9. The Committee noted that a number of previous recommendations had been made by the Special Foods Subcommittee regarding promoting the use of

Extensively Hydrolysed Formulas (EHF) as a first line option compared to Amino-acid Formula's (AAF). The Committee noted that changes had been made to the access criteria for Amino-acid Formula in 2020 to address this and considered that the majority of these actions could now be closed.

5.1.9.1. The Committee considered that the 2015 recommendation from the Special Foods Subcommittee that educational support be provided to prescribers regarding EHF and AAF in primary and secondary care to improve prescribing practice should remain open. Members considered that there was still a need for education as there was some confusion amongst prescribers regarding the access criteria and additional education and resources would be beneficial. Members considered that education should focus on interpretation and understanding of the access criteria and the benefits and risks associated with soy formulas.

5.1.10. The Committee considered the 2012 recommendation from the Special Foods Subcommittee that the access criteria for standard supplements be amended to exclude people with dementia and widened to include pregnant people with an eating disorder.

5.1.10.1. The Committee discussed that the recommendation to exclude people with dementia from the criteria for '*Severe chronic neurological conditions*' had arisen because of concerns at the time that people with dementia were inappropriately being prescribed standard supplements under this criterion. Members did not consider that current prescribing of standard supplements was inappropriate and did not consider that the exclusion of people with dementia was required.

5.1.10.2. The Committee considered that a health need remained for pregnant people with an eating disorder and the recommendation to widen access to standard supplements to include this group should remain open. The Committee noted that pregnant people with severe hyperemesis gravidarum who were unlikely to meet recommended nutritional or weight gain requirements were able to access standard supplements, however this did not include pregnant people with an eating disorder.

5.1.10.3. The Advisory Committee **recommended** the following changes to the criteria for standard supplements for short term medical conditions to include this group, additions in **bold** deletions in ~~strikethrough:~~

Initial application — (Short-term medical condition) from any relevant practitioner.
Approvals valid for 1 year for applications meeting the following criteria:
Any of the following:

1. Is being fed via a nasogastric tube or a nasogastric tube is to be inserted for feeding; or
2. Malignancy and is considered likely to develop malnutrition as a result; or
3. Is undergoing a bone marrow transplant; or
4. Temporomandibular surgery or glossectomy; or
5. Both:
   - 5.1. Pregnant; and
   - 5.2. Any of the following:
     - 5.2.1 Patient ~~is in early pregnancy (< 13 weeks) and~~ has severe clinical hyperemesis gravidarum requiring admission to hospital and is unlikely to meet nutritional requirements due to continuing hyperemesis gravidarum; or
     - 5.2.2 Patient has **disordered eating** ~~clinical hyperemesis gravidarum continuing past 13 weeks~~ and either there is concern that the patient is unlikely to meet the Institute of Medicine's (1990) recommended weight gain guidelines for pregnancy or the patient's weight has not increased past the booking/pre-pregnancy weight; or

5.2.3 Patient has a multiple gestation pregnancy and is under the care of an obstetric team who consider the nutritional needs of the patient are not being met.

Renewal — (Short-term medical condition) from any relevant practitioner. Approvals valid for 1 year for applications meeting the following criteria:
Any of the following:
1 Is being fed via a nasogastric tube; or
2 Malignancy and is considered likely to develop malnutrition as a result; or
3 Has undergone a bone marrow transplant; or
4 Temporomandibular surgery or glossectomy; or
5 Both:
5.1 Pregnant; and
5.2 Any of the following:
5.2.1 Patient ~~is in early pregnancy (< 13 weeks) and~~ has severe clinical hyperemesis gravidarum requiring admission to hospital and is unlikely to meet nutritional requirements due to continuing hyperemesis gravidarum; or
5.2.2 Patient has **disordered eating** ~~clinical hyperemesis gravidarum continuing past 13 weeks~~ and either there is concern that the patient is unlikely to meet the Institute of Medicine's (1990) recommended weight gain guidelines for pregnancy or the patient's weight has not increased past the booking/pre-pregnancy weight; or
5.2.3 Patient has a multiple gestation pregnancy and is under the care of an obstetric team who consider the nutritional needs of the patient are not being met.

5.1.10.4. The Committee considered that the number of pregnant people with an eating disorder who would access standard supplements was small but growing. Members discussed that pregnant people with severe eating disorders would be unlikely to access standard supplements. The Committee considered that the proposed changes would not result in any significant increase in the number of people accessing standard supplements but would make access easier for the people with the highest need.

5.1.11. The Committee noted the 2010 recommendation from the Special Foods Advisory Committee that national home delivery of Special Foods in New Zealand be implemented across New Zealand. The Committee noted information provided by Pharmac that direct distribution of Special Foods is within the scope of the Integrated Community Pharmacy Services Agreement, which is managed by Te Whatu Ora. The Committee noted that Pharmac staff had shared the request for direct delivery services with Te Whatu Ora and it was on their work programme but a timeline for resolution had not been provided.

5.1.11.1. . The Committee considered that the need for centralised, national delivery services for special foods remained and would be particularly beneficial in rural or isolated areas throughout New Zealand where access to special foods and pharmacies to dispense them could be difficult. Members considered this would offer significant benefit to priority populations, including Māori, who experience inequities in receiving funded healthcare in New Zealand.

5.1.11.2. The Committee noted that as a result of the COVID-19 pandemic there had been significant and continuing supply issues for Special Foods. The Committee considered that a centrally managed national distribution arrangement for Special Foods would help to minimise this and would help to ensure all people who need them would be able to access Special Foods in the event of supply issues.

5.1.11.3. Members noted that in addition to improving access, a national delivery service would also reduce costs to people using special foods by reducing discrepancies in the part charges and handling fees. Members considered that the implementation of these services would require collaboration across the health sector, including Pharmac and Te Whatu Ora.

5.1.11.4. The Committee recommended that a letter reiterating the need for national distribution of Special Foods should be sent from Pharmac on behalf of the Special Foods Advisory Committee to the Team at Te Whatu Ora responsible for managing the Integrated Community Pharmacy Agreement and copied to the Te Whatu Ora Chief Executive.

5.1.12. The Committee noted three outstanding actions related to funded food thickeners. The first two were recommendations in 2013 and 2017 by the Special Foods Advisory Committee that food thickeners be delisted from Section D of the Pharmaceutical Schedule on the basis that evidence did not support their use in this setting. The third recommendation was a recommendation from the Special Foods Advisory Committee in 2017 that a range of powder thickeners and pre-thickened fluids be listed in Section H of the Pharmaceutical Schedule for people with dysphagia diagnosed by a speech language therapist.

5.1.13. The Committee noted that Pharmac had recently undertaken a consultation regarding funding of food thickeners in the community and considered that these items could be reconsidered once the open consultation was resolved.

5.1.14. The Committee noted a 2010 recommendation from the Special Foods Advisory Committee that the Alfare brand of Extensively hydrolysed infant formula, supplied by Nestlé be listed on the Pharmaceutical Schedule. The Committee noted information provided by Pharmac that the item had been discontinued by the supplier and considered that this action point could be removed. Members considered that infant formulae should be renamed as paediatric formulae so that it was consistent with other listings on the Pharmaceutical Schedule.

5.1.15. The Committee noted a 2013 recommendation from the Special Foods Advisory Committee regarding the funding of PKU Lophlex Sensation 20 supplied by Nutricia. The Committee noted that PKU Lophlex Sensation20 had been listed on the Pharmaceutical Schedule in 2018 and considered that this item could be removed from the list of open actions.

5.1.16. The Committee noted a 2008 recommendation from the Special Foods Advisory Committee regarding the funding of a range of supplements for various inherited metabolic diseases supplied by Vitaflo. The Committee noted that Pharmac is currently in negotiations with Vitaflo regarding this, with an outcome expected in early 2024.

5.1.17. The Committee noted a 2006 recommendation that Pharmac should investigate the potential to enter into national contracts for giving sets – as some people were required to meet the cost of them. The Committee noted that medical devices are now being managed by Pharmac's Medical Devices Directorate and Te Whatu Ora and considered that this recommendation should be provided to them.

6. Update on funding decisions

6.1. Members noted that many of Pharmac's recent funding decisions for Special Foods had been to address supply issues resulting from the COVID-19 pandemic.

Members noted that overall supply issues had improved but were continuing for a number of products.

6.2. The Committee considered that to address these ongoing supply issues it would be helpful to have a greater number of alternative products funded, particularly where there is only one funded brand available, and where there have been significant out of stock situations or where products are used as a sole source of nutrition.

7. NPPA Review

7.1. The Committee noted that since its last meeting in December 2017, 122 applications had been received via Pharmac's Named Patient Pharmaceutical Assessment (NPPA) Pathway with all of these being initial applications. The Committee noted that a significant volume of the applications received during this period appear to have been for low calcium infant formula (Locasol brand) and a range of supplements for people with inherited metabolic diseases.

7.2. Members noted that low calcium infant formulas are currently funded specifically for infants with Williams Syndrome and associated hypercalcaemia. The Committee were uncertain why NPPA applications would be required for this product as it should be able to be accessed via the Pharmaceutical Schedule for people who need it. The Committee recommended that Pharmac review the NPPA applications to understand if they would fit under the existing Special Authority criteria or if there was a group that the criteria do not cover.

7.3. The Committee noted that Pharmac staff were negotiating supply agreements for a range of supplements for inherited metabolic diseases which would allow these supplements to be accessed via the Pharmaceutical Schedule and would mean that many NPPA applications for supplements for inherited metabolic diseases would no longer be required. It was noted that NPPA applications would continue to be assessed for supplements for inherited metabolic diseases while this process was completed.

7.4. The Committee noted that a number of NPPA applications had been received for supplements for paediatric kidney disease (Renastart brand). Members noted that there is currently only one funded supplement for children with chronic renal failure (Kindergen brand) which had experienced significant supply disruptions during the COVID-19 pandemic. This meant NPPA applications for Renastart were required to ensure a funded product was available.

7.5. Members noted that a relatively small proportion of the NPPA applications in the Special Foods Therapeutic Group were declined because the principles were not met and the majority of these appeared to be requests for standard enteral supplements.

8. Therapeutic Group Review

8.1. Expenditure Summary

8.1.1. The Advisory Committee noted that expenditure across the Therapeutic Group was relatively stable, with relatively small year on year growth. The Committee noted that the Oral and Enteral Feeds category contributed the majority of the expenditure in the Special Foods Therapeutic Group and the ongoing growth.

8.1.2. The Advisory Committee noted that the usage and expenditure information presented in the Therapeutic Group Review did not include usage by Te Whatu Ora Hospitals via the Hospital Medicines List (HML). The Advisory Committee considered it would be helpful to see this data as it considered

usage and expenditure in hospital settings could be significant. Members noted that Te Whatu Ora Hospitals were increasingly being asked to provide significant volumes of stock to people transitioning to community-based care and between hospitals due to supply issues and concern about people not being able to access sufficient stock. Members noted in some instances pharmacies and wholesalers did not stock a requested product and it could take time for this to be established.

Oral and enteral feeds

8.1.3. The Committee noted that usage and expenditure had been relatively stable in recent years. The Committee noted that the majority of the expenditure and growth in this subgroup is from oral feed powder 1kcal/ml. Members noted that this growth in expenditure would be expected to continue due to the ageing population in New Zealand. Members also noted that oral feed 1kcal/ml powders were also commonly mixed to 1.5kcal/ml concentrations, further increasing use of this product.

8.1.4. The Committee noted that that expenditure on oral feed powder 1kcal/ml significantly exceeded 1.5kcal/ml liquid options. The Committee considered that this was because oral feed powder, 1kcal/ml is the only fully funded option in this subgroup. The Committee noted that funded liquid options, (oral feed 1.5 kcal/ml and oral feed 1.5 kcal/ml with fibre) are fully subsidised by endorsement for identified patient populations only, which means that some people using these liquid supplements are required to pay the difference between the subsidised amount and the price charged at the pharmacy via a part charge.

8.1.5. The Committee noted that people meeting particular requirements were able to access fully funded oral feed 1.5 kcal/ml liquid supplements, including people being bolus fed through a feeding tube, people who have severe epidermolysis bullosa, or as exclusive enteral nutrition in children under the age of 18 years for the treatment of Crohn's disease, or for people with COPD with hypercapnia, defined as serum CO2 value exceeding 55mmHg.

8.1.6. The Committee noted that the majority of people using oral feed 1.5 kcal/ml liquid supplements were required to pay a part charge. The Committee considered that the proportion of people receiving partially funded and fully funded oral feed 1.5 kcal/ml liquid and oral feed 1.5 kcal/ml liquid with fibre had been relatively stable in recent years, with 34% of people receiving fully funded oral feed 1.5kcal/ml and 66% of people receiving partial funding in the 2022/23 Financial Year. For oral feed with fibre 1.5kcal/ml liquid 74% of people received full funding and 26% of people received partial funding.

8.1.7. The Committee noted information provided by Pharmac that the amount of the part charge for oral liquids has been set based on confidential pricing per ml for 1 kcal oral feed powder. Members noted that the decision to apply partial funding for liquid oral special foods had been implemented from 1 April 2011 to manage expenditure in the Special Foods Therapeutic Group. This decision had been made on the basis that people could access fully funded 1 kcal/ml oral feed powder or choose to pay a part charge to access 1.5kcal/ml liquid supplements. The Committee noted that the use of part charges in this instance had resulted in increased use of fully funded oral feed powder 1kcal/ml relative to 1.5kcal/ml liquid supplements.

8.1.8. The Committee considered that the use of part charges had reduced expenditure to Pharmac’s budget, however, concerns were raised regarding the ongoing use of partial funding for oral feed 1.5 kcal/ml liquid

supplements. The Committee considered that the use of part charges for these supplements in the community resulted in inequity of access. The Committee noted that based-on pricing in the Pharmaceutical Schedule the cost of the part charge to the patient would be $0.54 per bottle. However, pharmacies were able to choose the amount of the markup applied to the patient part charge. This meant the amount charged to people could vary significantly depending on the mark up applied by their pharmacy. Members considered that this resulted in significant and variable costs to people receiving part funded oral feed 1.5kcal/ml liquid supplements.

8.1.9. The Committee considered that the use of part charges for these supplements was resulting in inequities for people who may not have the resources and capacity to access and prepare fully funded 1 kcal/ml oral feed powder. This included people who did not have access to clean running water to prepare the liquid or a fridge to store it, and people with language barriers or literacy and numeracy comprehension challenges who may have difficulty preparing the supplement to the required concentration. Members considered that these barriers to access were resulting in negative health outcomes for some people, which could be addressed if they were able to access fully funded oral feed 1.5kcal/ml liquid supplements.

8.1.10. The Committee considered that these barriers were more likely to impact priority populations including Māori and Pacific peoples, people experiencing socioeconomic deprivation and disabled people.

8.1.11. Members also considered that the application of part charges for these supplements was not equitable on the basis of age, with paediatric oral supplements, recommended for use in people up to the age of 10 years being fully funded but people from 11 years of age and over being required to pay a part charge to access 1.5 kcal/ml oral liquid supplements.

8.1.12. The Committee noted that Pharmac was reviewing the use of part charges across the Pharmaceutical Schedule, which included the Special Foods Therapeutic Group.

8.1.13. The Committee noted that the removal of part charges from these supplements would result in additional expenditure to Pharmac's budget, which would need to be assessed and prioritised against the other options for investment being considered by Pharmac. Members noted that for this proposal to compare favourably, it would be important to identify the unmet health need in the current situation and the measurable health benefits that would be expected to result from full funding of 1.5 kcal/ml oral liquid supplements.

8.1.14. The Committee noted there was a preference amongst people using oral supplements for access to liquid rather than powdered supplements as they were more convenient. Members noted there was also a preference for liquid compared to powder supplements in paediatric settings as it was easier for children to travel and take pre-packaged liquid supplements to school.

8.1.15. Members estimated that if oral feed 1.5 kcal/ml liquid supplements were fully funded for all people who are currently able to access them, it would be expected that 70% of use would be oral feed 1.5 kcal/ml liquid supplements and the remaining 30% of use would be oral feed powder 1kcal/ml.

8.1.16. The Committee considered that while part charges were being considered more broadly, the amount of reference pricing for oral feed 1.5 kcal/ml liquid supplements and the way it is calculated should be reviewed by Pharmac to

ensure it remains in line with the cost of oral feed powder 1kcal/ml. The committee considered it would be appropriate to calculate on a per kcal basis rather than per ml.

8.1.17. The Committee also considered that the list of factors required for access to fully funded oral feed 1.5 kcal/ml liquid supplements was relatively limited and considered it would be helpful to review this list at a future meeting to make sure it remained appropriate.

Diabetic supplements

8.1.18. The Committee noted that the use and expenditure of funded diabetic supplements had been relatively stable.

8.1.19. The Committee noted the upcoming discontinuation of Nutrison Advanced Diason expected in early 2024. The Committee noted that a funded alternative Diabetic enteral feed 1kcal/ml was available (Glucerna Select brand) and other funded diabetic oral feed 1kcal/ml supplements are available which would be suitable alternatives for the currently funded population of people with diabetes requiring nutritional support. Members noted that it would be useful to have greater redundancy for 1kcal/ml enteral feeds in the event of supply issues.

8.1.20. Members noted that Nutrison Advanced Diason was the only enteral supplement available in New Zealand which was suitable for a vegan or plant-based diet as it did not contain animal products. The Committee noted that use of Nutrison Advanced Diason for people wanting or requiring a vegan diet was unfunded. Members considered that the discontinuation of Nutrison Advanced Diason would create an unmet health need for these people.

Fat modified products

8.1.21. The Committee noted that the use and expenditure of fat modified products had been relatively stable.

Paediatric products

8.1.22. The Committee considered that use and expenditure of paediatric products appeared to be appropriate.

8.1.23. Members noted that the use of peptide-based oral feed appeared to have increased in recent years. Members noted that they were aware of children with cerebral palsy being trailed on the product.

Paediatric products for children awaiting liver transplant, children with chronic renal failure and children with low energy requirements

8.1.24. The Committee noted that use and expenditure of paediatric products for children awaiting liver transplant, products for children with chronic renal failure and products for children with low energy requirements had been relatively stable and appeared appropriate.

Renal products

8.1.25. The Committee noted that use and expenditure on renal oral feed 1.8kcal/ml had increased significantly in 2021 and 2022 after a period of stability in previous years.

8.1.26. Members noted that this increased use was associated with supply issues with other funded renal supplements and this increased use would not be expected to continue.

Specialised and elemental products

8.1.27. The Committee noted that compared to other funded supplements Oral elemental feed 0.8kcal/ml (Elemental 028 brand) was significantly more expensive and use of this supplement appeared to have increased in recent years.

8.1.28. Members noted they were aware of Elemental Oral elemental feed 0.8kcal/ml being used in some instances where people required a plant-based diet, which may be contributing to increased expenditure in this category.

Food Thickeners in the Community

8.1.29. The Committee noted that the availability of food thickeners had been considered previously by the Special Foods Subcommittee on a number of occasions. The Committee noted that the most recent recommendation from the Special Foods Subcommittee had been in 2017 where the Subcommittee had recommended that Food Thickeners should not be funded in the community.

8.1.30. The Committee noted in February 2023 Pharmac had released a consultation on a proposal to phase out the funding of food thickeners in the community. The Committee noted that all of the responses were supportive of access being retained for the current group or widened to include other populations.

8.1.31. The Committee noted that the funding of food thickeners in the community and the responses received had been considered by the Pharmacology and Therapeutics Advisory Committee (PTAC) at its August 2023 meeting. The Committee noted that PTAC had recommended that access be retained the community for people with motor neurone disease with a swallowing disorder.

8.1.32. The Committee also noted that PTAC had also considered that further work be undertaken by Pharmac to better define the groups of people with persistent and progressive swallowing disorders, who would be considered to have an equivalent health need to the currently funded group with motor neurone disease. The Committee noted PTAC's consideration that this would likely include people with persistent and progressive swallowing disorders that lead to significant weight loss where surgical interventions such as a percutaneous endoscopic gastrostomy (PEG) are indicated to meet nutritional and/or hydration requirements, or people with similar presentations where PEG insertion is not possible.

8.1.33. The Committee noted that there is limited evidence available to support the use of food thickeners in the community. Members noted that food thickeners are often not tolerated well, and a significant number of people choose not to use them.

8.1.34. Members noted that inappropriate use of food thickeners could result in harm through increased risk of aspiration.

8.1.35. Members considered use of food thickeners has little impact on the nutrition a person is able to consume, and their benefit (if any) relates to safer swallowing.

8.1.36. Members noted that people who have had a stroke would be the largest group of people who may seek access to food thickeners if access was widened. Members noted that strokes do not typically result in progressive

dysphagia and this group would not be expected to have a health need that is equivalent to people with motor neurone disease.

8.1.37. The Committee considered that food thickener protocols in the community were unclear. Members noted that Speech Language Therapists would be closely involved in the decision to use food thickeners. Members also considered that neurologists were likely to care for a number of people using food thickeners and may be able to identify groups of people with the highest need.

8.1.38. The Committee noted that access to Speech Language Therapists, Neurologists and other specialist is likely to be challenging and inequitable across the country. The Committee did not consider that limiting access to food thickeners in the community to particular types of prescribers would be appropriate.

8.1.39. The Committee noted that the currently funded range of food thickeners were not preferred as it was difficult to achieve the desired thickness and the texture of these thickeners could be grainy. Members considered that newer thickeners such as those developed by Precise would be preferred.

Food and supplements for inherited metabolic diseases

8.1.40. The Committee noted that use and expenditure of Foods and Supplements for inherited metabolic diseases had been relatively stable and appeared appropriate.

Nutrient Modules

8.1.41. The Committee noted that use and expenditure of Nutrient Modules had been relatively stable and appeared appropriate.

Ketogenic diet

8.1.42. The Committee noted that use of funded supplements for a Ketogenic Diet had been relatively stable.

8.1.43. Members noted that currently funded supplements for a ketogenic diet (KetoCal 3:1 and Ketocal 4:1) are used in children with epilepsy and people with metabolic conditions and was further limited by the need for Special Authority applications to be from a metabolic physician or paediatric neurologist. Members considered that there was currently an unmet health need for adults with epilepsy and, possibly, people with cancer who may benefit from a ketogenic diet.

Gluten Free Foods

8.1.44. The Committee **recommended** that Pharmac should resume active management of funded gluten free foods for people with coeliac disease.

8.1.45. The Committee made this recommendation based on:

- Inequities and barriers to access that currently exist for people with coeliac disease requiring gluten free foods in New Zealand, which it was considered would have a significant impact on priority populations.

8.1.46. The Committee noted that gluten free food prescription numbers and Pharmac's expenditure on these had continued to decline in recent years. Members considered that this would have been in part influenced by Pharmac's April 2011 decision to stop actively managing gluten free foods, which had resulted in the funded range of gluten free foods available and their availability throughout the country reducing significantly.

8.1.47. The Committee considered that there were inequities of access regarding unfunded gluten free foods, which were easier to access in main urban centres but were not always available in more isolated parts of the country.

8.1.48. Members noted that the cost of gluten free foods compared to foods containing gluten presented a significant barrier to access for some people. The Committee discussed that some people were able to access a Child Disability Allowance or Disability Allowance to help meet the additional cost of gluten free foods, Members noted that this created additional inequities in access as some Healthcare Professionals considered people with Coeliac disease to qualify for a Disability Allowance while others did not. Members noted that a further barrier to access was the need for people to see a dietitian or general practitioner in order to receive a prescription for funded gluten free foods and the additional costs associated with this. Members considered that these barriers to access were likely to have the most significant impact on populations already experiencing health inequities in New Zealand including Māori and Pacific peoples, people experiencing socioeconomic deprivation, people residing in rural locations and people with lower levels of health literacy.

8.2. Horizon Scanning

Fortisip Compact Protein

Application

8.2.1. The Advisory Committee reviewed updated information regarding the current funding applications for Fortisip Compact Protein.

8.2.2. The Advisory Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

Recommendation

8.2.3. The Advisory Committee **recommended** that Fortisip Compact Protein be listed in Section D and Section H of the Pharmaceutical Schedule with a **high priority** alongside currently funded standard supplements

8.2.4. The Advisory Committee made this recommendation based on:

- Health benefits associated with improved adherence due to the lower volume of Fortisip Compact (2.4 kcal/ml) compared to currently available 1.5kcal/ml oral supplements.
- Improved suitability compared to currently available supplements due to a wider range of flavours.
- Consideration that the use of high calorie density, low volume feed is now the standard of care globally for people requiring oral nutritional supplements.

Discussion

8.2.5. The Committee noted that in October 2023 a letter of support for the ongoing funding of Fortisip Compact Protein in Section D and Section H of the Pharmaceutical Schedule had been received from the Te Whatu Ora Dietitians' Leadership Group. The Committee noted that the letter outlined benefits associated with the use of Fortisip Compact Protein that the Te Whatu Ora Dietitians' Leadership Group considered warranted a reconsideration of the cost neutral funding recommendations previously received for this product.

8.2.6. The Committee noted that the Te Whatu Ora Dietitians' Leadership Group's letter followed the receipt of a significant volume of correspondence from clinicians requesting the availability of Fortisip Compact Protein in the community and Te Whatu Ora Hospitals. The Committee noted that this correspondence had been provided to it for consideration.

8.2.7. The Committee noted that Fortisip Compact Protein has been temporarily available in Te Whatu Ora Hospitals since 2022 due to supply issues with other Special Foods Supplements as a result of the COVID-19 pandemic.

8.2.8. The Committee noted that Fortisip Compact Protein had been considered by the Special Foods Subcommittee on a number of occasions, in May 2010, September 2012 and July 2015. The Committee noted that on each of these occasions Fortisip Compact Protein had received funding recommendations of cost saving or cost neutral.

8.2.9. The Committee noted it was not aware of new published evidence regarding Fortisip Compact Protein or high-density low volume feeds becoming available following previous consideration by the Special Foods Subcommittee.

8.2.10. The Committee noted that Pharmac had been negotiating with the supplier of Fortisip Compact to achieve cost neutral pricing but that this had been unable to be achieved.

8.2.11. Members noted that the current price for a bottle of Fortisip Compact was $0.084 per kcal compared to $0.0042 for a fully funded bottle of 1.5kcal/ml oral liquid.

8.2.12. The Committee noted information in the Te Whatu Ora Dietitians' Leadership Group's letter regarding a survey undertaken in Waitematā hospital, which reported that of the people surveyed, the majority noted that they enjoyed this product more than other currently available oral nutritional supplements and were able to finish it more easily.

8.2.13. The Committee noted that Fortisip Compact Protein was nutritionally equivalent to currently funded 1.5kcal/ml liquid supplements, however, was available in a smaller volume of liquid of 125 ml per bottle compared to 200 ml per bottle.

8.2.14. Members considered that this smaller volume would offer a significant benefit to many people using oral supplements and particularly people using significant quantities who may struggle to consume the recommended volume of 1.5kcal/ml oral supplements.

8.2.15. Members considered that the lower volume of Fortisip Compact Protein could offer benefits to people using 1.5kcal/ml oral supplements by allowing them to consume the recommended volumes to meet their nutritional requirements. Members considered that some people were not currently meeting their nutritional requirements with currently funded supplements as they were unable to consume the required liquid volume.

8.2.16. Members noted that Fortisip Compact Protein was also available in a wider range of flavours than currently available 1.5kcal/ml liquid supplements, which could help to increase adherence.

8.2.17. Members noted that although it was currently available in Te Whatu Ora Hospitals, uptake of Fortisip Compact had been relatively low as it was not available in the community. This meant people were unable to continue

receiving it as they transitioned to community-based care, meaning people are often not started on this treatment in hospital.

8.2.18. Members considered that if Fortisip Compact was to be funded up to 70% of people currently receiving 1.5kcal/ml oral nutritional supplements would transition to it over 12 months of it first becoming available.

8.2.19. The Committee noted that there were other high density low volume liquid oral supplements available that were similar to Fortisip Compact Protein. Members considered that the nutritional composition and volume of these supplements is not equivalent, and therefore these supplements would not be considered equivalent to each other.

Plant based oral and enteral supplements

Agenda item

8.2.20. The Committee reviewed information regarding plant based oral and enteral supplements which are becoming available internationally.

Recommendation

8.2.21. The Committee **recommended** that Pharmac should engage with Nutricia regarding its possible funding application for plant-based supplements and the timing of when this could be expected to be received.

8.2.22. The Committee made this recommendation based on:

- The expected unmet health need for people who require plant based oral and enteral supplements but do not currently have funded options available.

Discussion

8.2.23. The Committee noted that Nutricia had recently launched plant based oral and enteral supplements internationally and expected to make these available in New Zealand in the near future. The Committee noted that Pharmac has not received an application for plant-based supplements to be funded via the Combined Pharmaceuticals Budget.

8.2.24. The Committee considered it was likely that oral and enteral plant-based supplements would be available from multiple suppliers over time. Currently the Committee noted that it was only aware of products manufactured by Nutricia.

8.2.25. The Committee noted that currently available data for plant based oral and enteral supplements was limited to two abstracts that were presented at the ESPEN congress in 2022.

- Griffen C, et al. Abstract no. ESPEN22-LB-2147. Presented at ESPEN Congress, Vienna, 3rd-6th September 2022.
- Delsoglio M, et al. Abstract no. ESPEN22-LB-2139. Presented at ESPEN Congress, Vienna, 3rd-6th September 2022

8.2.26. The Committee noted that there was an increasing number of people requesting access to plant-based alternatives to currently funded nutritional supplements. The Committee noted that following the imminent discontinuation of Nutrision Advanced Diason there would be no plant-based supplements available for people following a plant based or vegan diet. Members considered there would be an unmet health need for these people.

8.2.27. Members considered that suitable comparators when considering plant-based supplements would be elemental or modular feeds, which were currently being used by some people following a plant based or vegan diet.

8.2.28. The Committee considered that it would be challenging to define the group of people following a plant based or vegan diet who might request access to plant-based supplements. Members considered that the criteria for access would need to be the same or similar to the current criteria for standard supplements.

8.2.29. The Committee noted that the access criteria for plant based oral and enteral supplements would be considered at the time that a funding application is received for these supplements.

KetoCal 4:1 Liquid – Funding Application

Interests

8.2.30. The Advisory Committee reported no conflicts of interest with regard to this agenda item.

Agenda item

8.2.31. The Committee reviewed information regarding a funding application that had been received by Pharmac for KetoCal 4:1 Liquid

Recommendation

8.2.32. The Advisory Committee **recommended** that KetoCal 4:1 liquid be listed in Section D and Section H of the Pharmaceutical Schedule with a **low priority** for intractable epilepsy, pyruvate dehydrogenase deficiency or glucose transporter type-1 deficiency and other conditions requiring a ketogenic diet.

8.2.33. The Advisory Committee made this recommendation based on:

- The small health benefit that may arise for some people from having a liquid formulation of KetoCal 4:1 available, which may be easier to prepare and consume compared to powder KetoCal 4:1 and KetoCal 3:1.
- The relatively small unmet health need of people with intractable epilepsy, pyruvate dehydrogenase deficiency or glucose transported type-1 deficiency and other conditions requiring a ketogenic diet, who cannot tolerate or do not like using the currently funded powdered supplements.

Discussion

8.2.34. The Committee noted that in August 2020 Pharmac received a funding application from Nutricia for the liquid formulation of KetoCal 4:1. The funding proposal is for children and adults with intractable or drug-resistant epilepsy and other conditions/disorders where a Ketogenic Diet is indicated. The application indicates that the intention would be for KetoCal 4:1 Liquid to be available alongside the currently funded powder formulation.

8.2.35. The Committee noted that the applicant considered that KetoCal 4:1 Liquid may better address nutritional needs compared to the currently funded KetoCal 4:1 powder with the addition of fibre, preventing constipation and with a superior fatty acid profile including the addition of long chain polyunsaturated fatty acids (LCPs).

8.2.36. The Committee noted that as a premade liquid feed KetoCal 4:1 liquid would not require preparation by the person using the supplement or their whānau/family or carers.

8.2.37. The Committee noted that the price quoted by the applicant for KetoCal 4:1 liquid was significantly higher than the price of the currently funded powder.

8.2.38. The Committee considered that the availability of KetoCal 4:1 liquid may address a small unmet health need for people who have difficulties preparing the currently available powdered option or are unable to tolerate the currently funded powdered option.

8.2.39. The Committee considered that the availability of KetoCal 4:1 liquid would not offer any additional benefit to Māori or other people experiencing health inequities in New Zealand due to the availability of KetoCal4:1 powder.

8.2.40. The Committee considered that approximately two thirds of people receiving KetoCal4:1 for a ketogenic diet are tube fed.

8.2.41. The Committee did not consider that the funding of KetoCal 4:1 liquid would offer any suitability benefit compared to currently available KetoCal 4:1 powder. The Committee considered that for the majority of people KetoCal 4:1 liquid would require additional modification before it could be used as they require a different ketogenic ratio. This would mean that it's use would still require significant administrative effort. Members also noted that ketones would require monitoring twice daily.

8.2.42. The Committee considered it was likely that liquid supplements would be supplied with a significantly shorter shelf life than powdered options.

Competition for Special Foods

Discussion

8.2.43. The Committee considered it would be advantageous to retain additional competition for the supply of Special Foods in New Zealand, particularly for supplements where there was no competition or no other suppliers in the New Zealand market such as paediatric enteral feed with fibre 1kcal/ml, semi-elemental enteral feed 1kcal/ml and high protein enteral feed.

8.3. Supply issues and other identified alternatives

8.3.1. The Committee discussed that frequent supply issues following the COVID-19 pandemic are continuing to occur across the special foods therapeutic group.

8.3.2. The Committee noted the treatment algorithm that is being used by Pharmac to assist with the initial identification of alternatives in the event of supply issues.

8.3.3. The Committee did not consider that changes were required to this treatment algorithm.

9. Matters Arising: Renilon 4.0 for Individuals with kidney disease who are not on dialysis

Application

9.1. The Advisory Committee reviewed the application for Renilon 4.0 oral nutrition supplement for the nutritional management of adults and children with chronic kidney disease.

9.2. The Advisory Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

Recommendation

9.3. The Advisory Committee **recommended** that Renilon 4.0 be listed with a **high priority** for the nutritional management of children with chronic kidney disease or hospitalised with acute kidney disease within the context of treatment with special foods subject to the following Special Authority criteria:

Initial application only from a dietitian or relevant practitioner. Approvals valid for 3 years where the paediatric patient has chronic kidney disease stage 3, 4 or 5 or is hospitalised with acute kidney disease.

Renewal only from a dietitian or relevant practitioner. Approvals valid for 3 years for applications meeting the following criteria:

The treatment remains appropriate, and the patient is benefiting from treatment.

9.4. The Advisory Committee made this recommendation based on:

- The importance of preventing and/or treating malnutrition while maintaining low quantities of protein, phosphate, potassium and fluid volume, in the diet of children who have chronic kidney disease.
- The physical and emotional impact that tube-placement procedures and associated complications may have on children and their parents, whānau and/or caregivers; and the health benefits that can be experienced including more food freedom when using an oral nutrition supplement.
- The reduction of tube-feeding procedures and associated complications and the impact this will have on the healthcare system.
- The cost-savings of using Renilon 4.0 compared to double strength (ie 40% w/v) Kindergen to provide nutritional supplementation.

9.5. The Advisory Committee **recommended** that Renilon 4.0 be listed with a **medium** priority for the nutritional management of adults with acute or chronic kidney disease within the context of treatment with special foods subject to the following Special Authority criteria:

Initial application only from a dietitian or relevant practitioner. Approvals valid for 3 years where patient has chronic kidney disease stage 4 or 5 or is hospitalised with acute kidney disease.

Renewal only from a dietitian or relevant practitioner. Approvals valid for 3 years for applications meeting the following criteria:

The treatment remains appropriate, and the patient is benefiting from treatment.

9.6. The Advisory Committee made this recommendation based on the importance of preventing or treating malnutrition, while maintaining low quantities of protein, phosphate, potassium and fluid volume, in adults who have chronic kidney disease.

9.7. The Advisory Committee requested the Nephrology Advisory Committee review and provide a view on the clinical value of low protein diets for children and adults with CKD.

Discussion

Background

9.8. The Committee noted that in 2012 the Special Foods Subcommittee (now the Special Foods Advisory Committee) noted that Renilon 4.0 was not used at the time and had the same, or similar, therapeutic effect to Suplena (see below). At the time, the Subcommittee considered that it should not be included in the National Hospitals Preferred Medicines List unless it was also listed in Section D (Special Foods) of the Pharmaceutical Schedule as otherwise there would be no continuity of access to treatment for people moving back into the community. The application was declined by Pharmac in May 2013.

9.9. The Committee noted in 2012 the Special Foods Subcommittee recommended Suplena liquid (a low electrolyte oral feed 2 kcal/ml containing 3 g protein, 25.5 g carbohydrate and 9.6 g fat per 100 ml) be included on the national Preferred Medicines List and listed under Section D (Special Foods) of the Pharmaceutical Schedule for acute or chronic renal failure under a combined Special Authority. Suplena was delisted from 1 February 2015 as it was discontinued by the supplier.

Health need

9.10. The Committee noted that CKD affects multiple metabolic pathways and people experience uraemia, electrolyte and acid-base imbalances, water and salt retention, mineral and bone disorders. The Committee noted a person with CKD can experience an altered appetite, taste profile and/or nausea resulting in difficultly eating enough food to meet their daily energy requirements (MacLaughlin et al. Am J Kidney Dis. 2022;79:437-44).

9.11. The Committee noted the Tafuna'i et al. Nephrology (Carlton). 2022;27:248-59 study which retrospectively reported the prevalence of CKD to be 13% among a cohort of people who were tested for CKD across two Auckland based health care centres. The Committee noted the older Lloyd et al. Nephrology. 2019; 24:308-15 study which reported the prevalence of CKD to be 11.8% among a cohort of people who were tested for CKD in the Otago-Southland region.

9.12. The Committee noted that both New Zealand studies reported the prevalence rate of CKD to be higher among Māori compared to non-Māori, non-Pacific peoples (Lloyd et al. Nephrology. 2019; Tafuna'i et al. Nephrology (Carlton). 2022). The Committee noted the incidence rates of end-stage kidney disease are greater among Māori (0-24 years old) compared to non-Māori, non-Pacific peoples of the same age (ANZDATA. 2022).

9.13. The Committee noted that both New Zealand studies reported the prevalence rate of CKD to be higher among Pacific peoples compared to non-Māori, non-Pacific peoples (Lloyd et al. Nephrology. 2019; Tafuna'i et al. Nephrology (Carlton). 2022). The Committee noted the incidence rates of end-stage kidney disease are greater among Pacific peoples (0-24 years old) compared to non-Māori, non-Pacific peoples of the same age (ANZDATA. 2022).

9.14. The Committee noted that when energy and nutritional intake from food alone is inadequate, nutritional supplementation is used to alleviate the risk of or treat malnutrition. The Committee noted that malnutrition is associated with poorer health outcomes and interventions are critical for the persons livelihood (MacLaughlin et al. Am J Kidney Dis. 2022;79:437-44).

9.15. The Committee noted that adults with stage 4-5 CKD and acute kidney disease can require less phosphorous, potassium, protein, and or liquid volume in comparison to people without CKD. The Committee noted special considerations for people with CKD when selecting feeds include ensuring there is adequate energy and appropriate protein intake provided, as well as electrolyte modification, depending on the individual's eGFR and serum electrolyte levels. If fluid restrictions and/or electrolyte modification is required, nutrient-dense, lower-volume, or kidney-specific products should be considered.

9.16. The Committee noted that children with stage 4-5 CKD or acute kidney disease require dietary modifications to mitigate the effects of impaired renal function, electrolyte abnormalities and malnutrition. In children, in addition to preventing delays in their growth, it is also important to ensure they do not become over nourished (leading to obesity), as a large decrease or increase in body mass index (BMI) are both associated with increased mortality risk from CKD (Thomas et al. Curr Treat Options Peds.2020;6:38-51).

9.17. The Committee noted that current options listed on the Pharmaceutical Schedule for adults with chronic or acute kidney disease who are not on dialysis and require nutritional supplementation include Renilon 7.5, Nepro and NovaSource Renal. The Committee considered these currently available products to be high in protein which may limit a person's other food choices and their ability to enjoy meals with family, whānau, caregivers or friends.

9.18. The Committee considered there to be approximately 100 adults who would use Renilon 4.0 if it was to be listed. The Committee considered there to be greater number of Māori and Pacific people compared to non-Māori, non-Pacific people who would benefit from listing of Renilon 4.0.

9.19. The Committee noted that Kindergen is currently listed on the Pharmaceutical Schedule for children with chronic or acute kidney disease who require nutritional management. The Committee noted Kindergen is an unflavoured powder that is made up at 20% or 40% (w/v) strength with water to meet the child's nutrition needs. The Committee considered that as Kindergen is made up by parents, whānau or caregivers, there is some risk that the formula is constituted at the incorrect concentration resulting in negative health outcomes (electrolyte imbalances, uraemia, impaired growth or excess weight gain) for the child being treated.

9.20. Members noted Kindergen is not palatable and is usually given via a nasogastric or a gastrostomy tube. Use of a gastrostomy tube requires an invasive procedure for insertion, with associated risks and complications. The Committee noted long-term nasogastric tubes are replaced at least every 2 months and gastrostomy tubes/balloons are initially placed during surgery and changed every 6-12 months.

9.21. The Committee considered that the placement, management and associated complications of the tubes may be associated with significant trauma for a child and their family or whānau, as they can interfere with swallowing and speech development, and can result in alteration to the appearance of the child. Common side effects are gastroesophageal reflux disease, vomiting and feeding tube aspiration and rarely oesophageal or gastric perforation might occur (Rees et al. Pediatr Nephrol. 2010;25:699-704).

9.22. The Committee noted there are approximately 20 children who are currently using Kindergen and considered there to be approximately 5 additional children who require an oral nutrition supplement, but for whom tube feeding is not appropriate. The Committee considered approximately 35% of children using Kindergen would use Renilon 4.0 if it was to be listed. The Committee noted that Renilon 4.0 is not currently recommended for children under the age of 3 years and expected that these children would continue to use Kindergen. Members also noted that there would also be a small number of children who would not accept oral supplements and would continue to require tube feeding to meet their nutritional requirements. The Committee considered there to be more Māori and Pacific children compared to non-Māori, non-Pacific children who would benefit from listing Renilon 4.0 as there was a higher proportion of Māori or Pacific children with CKD compared to other children for CKD in New Zealand.

9.23. The Committee considered that people with CKD with malnutrition require long-term management prior to transplantation or renal-replacement therapies or death. the Committee noted that Renilon 4.0 would also be required for short-term management of diet for people with acute kidney disease.

Health benefit

9.24. The Committee noted that Renilon 4.0 is a ready to drink, low protein, low electrolyte oral nutrition supplement formulated to be an appropriate nutritional supplement for people with renal failure requiring protein restriction.

9.25. The Committee noted the Kidney Disease Outcomes Quality Initiative (KDOQI) and The Academy of Nutrition and Dietetics guidelines for adults with CKD (Ikizler et al. Am J Kidney Dis. 2020; 76:S1-S107).

9.25.1. The Committee noted the recommendation that adults with CKD stage 3-5 who are metabolically stable, under close clinical supervision, use protein restriction with or without the addition of keto acid analogues to help manage and reduce the negative health effects associated with their CKD. The Committee noted the identified health benefits were a reduction in risk for end-stage kidney disease/death (strong recommendation based on high quality evidence) and improvement in quality of life (weak recommendation based on moderate quality evidence).

9.25.2. The Committee noted a low protein diet was defined as 0.55–0.60 g dietary protein/kg body weight/day, or a very low-protein diet providing 0.28–0.43 g dietary protein/kg body weight/day with additional keto acid/amino acid analogues to meet protein requirements (0.55–0.60 g/kg body weight/day).

9.25.3. The Committee noted the opinion-based recommendation that for adults with CKD 3-5 and diabetes, it is reasonable to prescribe, under close clinical supervision, a dietary protein intake of 0.6-0.8 g/kg body weight per day to maintain a stable nutritional status and optimise glycaemic control.

9.25.4. The Committee noted the previous recommendation was for adults without diabetes to consume 0.8 g/kg/day of protein and considered the protein restriction recommendations difficult to achieve without intense dietary education and restriction without the use of an oral nutrition supplement.

9.25.5. The Committee noted that that for adults with CKD 3-5, the guidelines recommend adjusting dietary phosphorus intake to maintain serum phosphate levels in the normal range (strongly recommended with moderate quality evidence).

9.25.6. The Committee noted the opinion-based recommendation that for adults with CKD 3-5 or post transplantation, it is reasonable to adjust dietary potassium intake to maintain serum potassium within the normal range.

9.26. The Committee noted the National Institute for Health and Care Excellence. Chronic Kidney Disease: Assessment and Management. NG203. London NICE 2021 guidelines which in 2014 advise against the intake of dietary protein intake less than 0.6 to 0.8 g/kg/day for adults with CKD.

9.27. The Committee noted the following studies:

9.27.1. Hahn et al. Cochrane Database Syst Rev. 2020;10:CD001892

9.27.2. Jiang et al. Cochrane Database Syst Rev. 2023;1:CD014906

9.28. The Committee considered that, protein restriction in adults may delay progression to end-stage kidney disease and may improve a person's quality of life (Ikizler et al. Am J Kidney Dis. 2020; 76:S1-S107). The Committee also considered that Renilon 4.0 would help prevent malnutrition that may be caused by a low-protein diet using foods alone, as well as reduce fatigue and hunger. The Committee considered that the prevention, or alleviation, of malnutrition to be clinically meaningful to the patient and individual's family and whānau. The Committee considered the formulation of Renilon 4.0 to appropriately support nutritional management of adults with CKD.

9.29. The Committee noted the Kidney Disease Outcome Quality Initiative (KDOQI) guidelines for children with CKD (KDOQI Work Group. Am J Kidney Dis. 2009;53:S11-104):

9.29.1. The Committee noted there are few randomised control trials of nutrition products involving children with CKD.

9.29.2. The Committee noted that supplemental nutritional support should be considered when the usual dietary intake of a child with CKD stages 2 to 5 or 5D fails to meet their energy requirements and the child is not achieving expected rates of weight gain and/or growth for age. The Committee noted that oral intake of an energy-dense diet and commercial nutritional supplements should be considered the preferred route for supplemental nutritional support for children with CKD stages 2 to 5 and 5D. When energy requirements cannot be met with oral supplementation, tube feeding should be considered. The Committee noted these recommendations were made with moderate quality evidence.

9.29.3. The Committee noted the opinion-based recommendation to maintain dietary protein intake at 100% to 140% of the dietary reference intake for ideal body weight in children with CKD stage 3 and at 100% to 120% of the dietary reference intake in children with CKD stages 3 to 5.

9.29.4. The Committee considered this guideline to be used when children are metabolically stable, when a child with stage 4-5 CKD is experiencing uraemia, the dietitian will prescribe a low protein diet of 0.4-0.5 g of protein per kg of body weight.

9.29.5. The Committee noted the expert opinion-based recommendations for children with CKD stages 3 to 5 and 5-dialysis, reducing dietary phosphorus intake to 100% of the daily recommended intake for age is suggested when the serum parathyroid hormone (PTH) concentration is above the target range for CKD stage and the serum phosphorus concentration is within the normal reference range for age. The Committee noted the recommendation to reduce dietary phosphorus intake to 80% if serum parathyroid hormone exceed the normal reference range.

9.29.6. The Committee noted it was strongly recommended that potassium intake needs to be limited for children with CKD stages 2 to 5 and 5D who have or are at risk of hyperkalaemia.

9.30. Members considered that the emphasis on reducing protein intake in people with CKD and noted emerging evidence that only diets that are very low in protein (0.3-0.4 g of protein per kg of body weight may offer benefits to people with CKD, and low protein diets (0.6-0.8 g of protein per kg of body weight) may not be associated with benefits to the person with CKD. Members noted that typically the use of supplements such as Renilon 4.0 would be used to achieve moderate protein intake of 0.8- 1 g of protein per kg of body weight or lower (0.3-0.4 g of protein per kg of body weight) for adults with acute CKD, or CKD 4 or 5.

9.31. Members considered that the listing of Renilon 4.0 would allow people to be treated in accordance with clinical guidelines for the treatment of CKD. Members noted that compared to other funded supplements Renilon 4.0 would provide a lower protein option compared to Renilon 7.5 and appropriate potassium and phosphate levels compared to available standard supplements.

9.32. The Committee noted the guidelines have not been updated since 2009 and invited the Nephrology Advisory Committee to provide feedback on the restriction of dietary protein in adults and children with CKD.

9.33. The Committee considered the replacement of Kindergen with Renilon 4.0 would provide significant health benefit for an affected child and their family, whānau or caregivers, without the need for tube feeding.

Suitability

9.34. The Committee noted Renilon 4.0 is an energy dense and low volume supplement so is suitable for people who require fluid restriction. It is also low in protein which helps prevent a person with CKD from experiencing an overload of nitrogenous waste products in their body, due to their impaired renal excretion of these. The Committee considered these qualities allow an individual with CKD to consume a greater proportion of their daily restricted protein intake from usual dietary food, which helps both provide them with variation in their diet and improves their satisfaction with the food choices available.

9.35. The Committee noted that the taste profile of Renilon 4.0 has been developed to be appetising to people with CKD when they are experiencing uraemia and considered this to be helpful to people when they are experiencing significant nausea or altered taste sensation.

9.36. The Committee noted that Renilon 4.0 would not be used in children under the age of 3 and these children would continue to require Kindergen.

9.37. The Committee noted that because Renilon 4.0 can be taken orally, children aged 3 years and over would not require a nasogastric or gastrostomy tube and would not require admissions to hospital to undergo the procedures/management of the complications associated with these tubes. Moreover, caregivers would not need to manage the tubes and the feeds and their complications.

Cost and Savings

9.38. The Committee considered that children and adults with CKD would require two bottles of Renilon 4.0 per day, with treatment required over the life course or until renal replacement therapy. The Committee considered it difficult to determine the average length of use between stage 4 and renal replacement therapies as the CKD progression is not linear. In CKD progression can be triggered in children following periods of growth, such as puberty.

9.39. The Committee considered that the reduction in the need for children to receive feeding tube-related procedures may reduce health-sector expenditure from hospital stays, procedure costs, clinician and nursing costs, and treatment of side-effects and complications.

9.40. The Committee considered Renilon 4.0 would replace Kindergen used at twice the strength for children and Renilon 7.5, Nepro or NovaSource for adults. The Committee noted other available macronutrient supplements can be used as required and a modular feed composed from the various macronutrient components available on the Schedule may be used for those for whom a ready-made product does not meet all nutritional requirements. Those currently listed on the Pharmaceutical Schedule are carbohydrate, fat, carbohydrate and fat and protein supplements.

Summary for assessment

9.41. The Advisory Committee considered that the table below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for [the pharmaceutical] if it were to be funded in New Zealand for [the indication]. This PICO captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO is based on the Advisory Committee's assessment at this time and may differ

from that requested by the applicant. The PICO may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

Population	Children with CKD	Adults with CKD, non-dialysis
Intervention	Renilon 4.0	Renilon 4.0
Comparator(s) (NZ context)	Kindergen	Renilon 7.5 Nepro
Outcome(s)	Possible improved health-related quality of life from oral treatment	Slowed progression of CKD and possible improved health-related quality of life related to being able to consume a wider variety of foods without exceeding protein recommendations.

Table definitions:
Population: The target population for the pharmaceutical, including any population defining characteristics (eg line of therapy, disease subgroup)
Intervention: Details of the intervention pharmaceutical (dose, frequency, treatment duration/conditions for treatment cessation).
Comparator: Details the therapy(s) that the target population would receive currently (status quo – including best supportive care; dose, frequency, treatment duration/conditions for treatment cessation).
Outcomes: Details the key therapeutic outcome(s), including therapeutic intent, outcome definitions, timeframes to achieve outcome(s), and source of outcome data.

10. Phlexy-Vits and Fruitivits for epilepsy treated with a ketogenic diet and inherited metabolic diseases

Application

10.1. The Advisory Committee reviewed the application for Phlexy-Vits and FruitiVits for ketogenic diet in the setting of epilepsy treatment, and inherited metabolic diseases (IEM).

10.2. The Advisory Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

Recommendation

10.3. The Advisory Committee recommended that Phlexy-Vits and FruitiVits be listed with **high priority** within the context of treatment with special foods, subject to the following Special Authority criteria:

> Multivitamins (Phlexy-Vits, FruitiVits)
> Initial application – Applications from any relevant practitioner. Approvals valid without further renewal unless notified.
> Either:
> 1. The patient has inherited metabolic diseases; or
> 2. The patient has epilepsy treated with a ketogenic diet.

10.4. The Advisory Committee considered the following in making this recommendation:

- The lack of funded low-carbohydrate micronutrient supplements for people with IEM and people with epilepsy requiring a ketogenic diet.
- The unmet health need of people with IEMs who are on a restrictive diet and people with epilepsy treated with a ketogenic diet.
- That people who are not on supplements are at risk of developing vitamin and mineral deficiencies eg vitamin A, B12 and D, iron and zinc.

- There are no currently funded vitamin and mineral supplements that would allow the use of macronutrient modules as sole nutrition or nutrition supplement for those affected.

Discussion

Māori impact

10.5. The Committee discussed the impact of funding Phlexy-Vits and FruitiVits for people with epilepsy treated with a ketogenic diet or IEMs on Māori health areas of focus and Māori health outcomes. The Committee considered that due to the small group size it was difficult to quantify the impact on Māori health outcomes.

Impact on Pacific peoples, disabled people, tāngata whaikaha Māori, and other people who have been underserved by the health system

10.6. The Committee discussed the impact of funding Phlexy-Vits and FruitiVits for people with epilepsy treated with a ketogenic diet or IEMs on Pacific, disabled, and underserved populations. The Committee considered that the small group size meant that it was hard to quantify if there were groups that experienced inequities and what the impact on them would be.

Background

10.7. The Committee noted that it had recommended the application for Phlexy-Vits and FruitiVits for children on a ketogenic diet for epilepsy be declined in 2017. The Committee noted that the rationale for this recommendation was that KetoCal used in the ketogenic diet contains micronutrients that would be supplemented by Phlexy-Vits or FruitiVits and children who are maintained on food based ketogenic diets do not require supplementation and the high cost of the product.

Health need

10.8. The Committee noted that people with IEMs likely to access Phlexy-Vits and FruitiVits if they were to be listed included people with phenylketonuria (PKU), glucose transporter type-1 (GLUT1) deficiency syndrome, glutaric aciduria type 1 (GA1) and pyruvate dehydrogenase deficiency. The Committee considered that there would be three people with GLUT1 deficiency syndrome, one to two with GA1 that require a ketogenic diet and would require micronutrient supplementation. The Committee considered that people with PKU who are using Phlexy10 tablets would also require supplementation as well as other people with IEMs following restrictive diets that require micronutrient supplementation to meet nutritional requirements. The Committee considered that this would be a small number of people.

10.9. The Committee considered that the small group size of both groups (IEM and epilepsy treated with ketogenic diet) meant that it was hard to quantify if there were specific groups that experienced inequities. The Committee considered that due to the small group size it was difficult to quantify Māori health outcomes.

10.10. The Committee considered that individuals with IEMs who are on a restrictive diet had an unmet health need, as there is a lack of funded low-carbohydrate micronutrient supplements for these people and this put them at risk of developing vitamin and mineral deficiencies eg vitamin A, B12 and D, iron and zinc. The Committee considered that there was an unmet health need for people with epilepsy on a ketogenic diet where KetoCal doesn't meet micronutrient requirements and there are no funded low carbohydrate options.

10.11. The Committee considered that with currently funded macronutrient modules there are no vitamin and mineral supplements that would allow the use of these as sole nutrition or nutrition supplement for people with epilepsy being treated with a ketogenic diet.

10.12. The Committee noted that ketogenic diet products that are nutritionally complete including micronutrients (KetoCal) are currently funded for people with epilepsy treated with a ketogenic diet, pyruvate dehydrogenase deficiency or GLUT-1 deficiency and other conditions requiring a ketogenic diet. The Committee considered that not all people with epilepsy on a ketogenic diet use KetoCal as their sole nutrition, with some people using food solely or supplementing with KetoCal. The Committee considered that one third of people using funded KetoCal would not be able to meet their micronutrient requirements and there were no funded, carbohydrate free micronutrient supplements for this group.

10.13. The Committee noted that Phlexy10 (amino acid formula without phenylalanine) tablets are currently funded as a protein supplement for people with IEMs and are intended for use in people with PKU where liquid formulations are not appropriate or accepted by the person being treated. The Committee noted that Phelxy10 tablets do not contain any vitamins, minerals or trace elements and if a person uses this as a sole source, or significant portion of their nutrition then the person would require a micronutrient supplement. The Committee considered that there were very few people using Phelxy10 tablets as sole or significant portion of their protein supplementation.

10.14. The Committee noted that there is a currently funded micronutrient powder (Paediatric Seravit) for people with IEMs. The Committee noted that Paediatric Seravit has a high carbohydrate content that makes it unsuitable for people on ketogenic diets and this was formulated for children and was not an appropriate option for adults. The Committee considered that Phlexy-Vits and Paediatric Seravit are comparable with regard to meeting nutrient reference values (NRV) for children under 15 years. The Committee noted that Phlexy-Vits does not contain choline, has higher vitamin B12 content and biotin content than the recommended daily intake (RDI) for children. The Committee considered that at the recommended dose of Phlexy-Vits, the upper tolerable intake level for magnesium is exceeded for children aged 1 to 10 years and exceeded for folate in children 10 to 15 years. The Committee noted that for individuals aged over 15 years, Phlexy-Vits meets more RDIs of vitamins, minerals and trace elements for this age group than ‘over the counter’ alternatives. The Committee noted that Pharmac assessments do not consider privately purchased products, such as those available ‘over the counter’, and that the comparator would be no micronutrient supplementation.

10.15. The Committee noted that there are funded individual vitamin and mineral formulations (zinc, B vitamins, multivitamin, vitamin C, vitamin D, iron, etc.) however, considered that these are inappropriate due to the volume of supplements that would be required or due to inappropriate doses.

Health benefit

10.16. The Committee noted that Phlexy-Vits is a low carbohydrate, concentrated vitamin, mineral and trace element powder used in restrictive therapeutic diets to meet micronutrient requirements. The Committee noted that the National Metabolic Service requested FruitiVits be considered in addition to Phlexy-Vits for children who are unable to use Phlexy-Vits.

10.17. The Committee noted that the dosing of FruitiVits and Phlexy-Vits vary based on the age, weight and condition of the person being treated. The Committee considered that the Phlexy-Vits dose for children under 10 years of age was roughly 40% to 60% of a sachet. The Committee considered that the FruitiVits dose was one sachet per day for those under 11 years and one and a half sachets per day for those aged over 11 years.

10.18. The Committee considered that compared to Phlexy-Vits, FruitiVits better meets the micronutrient requirements of children over 3 years as it contains choline to meet RDI, substantially more vitamin B12 and biotin than RDI as well, but an acceptable amount of magnesium and folate.

10.19. The Committee noted that the Pharmaceutical Benefits Advisory Committee (PBAC) in Australia recommended FruitiVits for those 3 years and older who have insufficient vitamin and mineral intake due to specific diagnoses requiring high restrictive therapeutic diet, where they are unable to adequately meet their vitamin, mineral and trace element needs with other proprietary vitamin and mineral preparations. The Committee noted that PBAC declined an application to fund FruitiVits for children younger than 3 years as it does not meet iron requirements.

10.20. The Committee considered that for people with IEMs following lifelong restrictive diets low bone mineral density is of particular concern as they may not receive adequate levels of micronutrients. The Committee considered that these diets may need to be stopped intermittently due to concerns around micronutrient deficiencies and maintaining safe levels of bone mineral density. The Committee considered that this is particularly important for children in periods of growth.

10.21. The Committee noted an open intervention study in 15 subjects aged 8 to 33 receiving Phlexy-Vits tablets assessing the acceptability, safety and impact on biochemical and haematological micronutrient status for 12 months (MacDonald et al. J Inherit Metab Dis. 2008; 31:718-23). The Committee noted that there were improvements in serum B12, manganese and glutathione peroxidase (GSHPx). The Committee considered that GSHPx is not a clinically useful marker and was not used in practice.

10.22. The Committee noted a post-hoc analysis of a randomised control trial comparing type of ketogenic diets in children 2 to 16 years (*N*=91) (Christodoulides et al. J Hum Nutr Diet. 2012;25:16-26). The Committee noted that during the 12-month study period children were supplemented with different micronutrient supplements including Phlexy-Vits including ten children initially but seven at the end of the study. The Committee considered that this may be because the palatability of the Phlexy-Vits is poor. The Committee considered changes in plasma vitamins A and E and the decline in magnesium status after 12 months of ketogenic diet treatment suggest that micronutrient status may be suboptimal in this group and that available formulations for ketogenic diet supplementation may need reviewing.

10.23. The Committee noted an open prospective study with 14 participants with restricted diets using FruitiVits for 26 weeks, assessing the impact on plasma nutritional biochemistry, height, weight and food frequency (Daly et al. J Hum Nutr Diet. 2016;29:434-40). The Committee noted that there was a significant improvement from baseline for folate, vitamin E, plasma selenium and total vitamin D. The Committee noted that 37% of the product remained unused.

10.24. The Committee considered that the strength and quality of the evidence is poor due to low numbers of participants in the studies. The Committee considered that it was unlikely that evidence of better quality and strength would be published. The Committee considered that it was biologically plausible that these supplements would provide a benefit by preventing, or reducing, vitamin and mineral deficiencies and the associated negative health effects. The Committee considered that it was difficult to quantify and extrapolate long term health outcomes from changes to micronutrient status, as there was a lack of evidence to inform such outcomes. The Committee considered that in general, severe micronutrient deficiencies may be associated with impaired health-related quality of life but that there was little evidence to inform this in people with in-born errors of metabolism or those using a ketogenic diet for treatment of epilepsy.

Suitability

10.25. The Committee noted that Phlexy-Vits are powder sachets able to be dissolved in water, to make a liquid or a paste. The Committee considered that the reconstituted liquid was less likely to cause tube blockage.

10.26. The Committee noted that for children younger than 11 years the recommended dose of Phlexy-Vits is part of a sachet and opened sachets should be stored in an airtight container and used in two to three days. The Committee noted that the supplier provided dosing for children one year and over however, this product is recommended by the manufacturer for use in people 11 years and over.

10.27. The Committee considered that FruitiVits are available in a sachet to be added to water, shaken to dissolve and consumed immediately. The Committee noted that FruitiVits are orange flavoured and intended for use in children 3 years and over.

Cost and savings

10.28. The Committee considered that Phlexy-Vits would be used among individuals aged 11 years and older at a dose of one sachet daily.

10.29. The Committee considered that FruitiVits could be used in children aged 11 years and younger at a dose of one sachet daily, and among individuals aged 11 and older at a dose of one and a half sachets per day.

10.30. The Committee considered that use of half sachets may result in wastage of the product if the other half of the sachet was discarded after administering the recommended daily dose.

10.31. The Committee considered that if Phlexy-Vits and FruitiVits were to be funded, the numbers of people receiving Phlexy10 may increase due to the recommended complement product, Phlexy-Vits, being funded. The Committee noted that the Pharmac dispensing data showed that over the past 10 years, very few people have been dispensed Phlexy10 tablets in the community. The Committee noted that the National Metabolic Service considered that there was at least one person receiving Phlexy10 as their sole protein nutrition. The Committee noted that the range of currently funded liquid and powder supplements for people with PKU and other IEMs, which already contain sufficient macronutrients, it was not expected that uptake of Phlexy10 would be significant.

Funding criteria

10.32. The Committee considered that criterion 1 (people with IEM) included people with PKU who may be using Phlexy10 tablets and this did not require an additional criterion.

10.33. The Committee considered that people with epilepsy treated with a ketogenic diet should also be included in the criteria for funding.

Summary for assessment

10.34. The Advisory Committee considered that the table below summarises its interpretation of the most appropriate PICOs (populations, interventions, comparators, outcomes) information for Phlexy-Vits and FruitiVits if it were to be funded in New Zealand for epilepsy treated with a ketogenic diet and IEMs. The PICOs capture key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. The PICOs are based on the Advisory Committee's assessment at this time and may differ from that requested by the applicant. The PICOs may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

Population	Individuals with inherited metabolic diseases (IEM) consuming a restrictive diet, for whom other funded powdered micronutrient supplements are not suitable.

Intervention	Phlexy-Vits, 7g dose per day In combination with a restrictive diet Duration of diet is indefinite, provided it is well tolerated and meeting an individual's nutritional requirements.	FruitiVits, 6g dose per day In combination with a restrictive diet Duration of diet is indefinite, provided it is well tolerated and meeting an individual's nutritional requirements.
Comparator(s) (NZ context)	Restrictive diet, without micronutrient supplementation Duration of diet is indefinite, provided it is well tolerated and meeting an individual's nutritional requirements.	
Outcome(s)	Prevention of micronutrient deficiencies including one or more of the following • Selenium • Calcium • Iron • Vitamin D • Vitamin E • Zinc Reduced risk of developing low bone mineral density	

Population	Individuals with epilepsy consuming a ketogenic diet, for whom other funded powdered micronutrient supplements are not suitable.	
Intervention	Phlexy-Vits, 7g dose per day In combination with a restrictive diet Duration of diet between two to three years, provided it is well tolerated and meeting an individual's nutritional requirements.	FruitiVits, 6g dose per day In combination with a restrictive diet Duration of diet between two to three years, provided it is well tolerated and meeting an individual's nutritional requirements.
Comparator(s) (NZ context)	Ketogenic diet, without micronutrient supplementation Duration of diet between two to three years, provided it is well tolerated and meeting an individual's nutritional requirements.	
Outcome(s)	Prevention of micronutrient deficiencies including one or more of the following micronutrients • Selenium • Calcium • Iron • Vitamin D • Vitamin E • Zinc Reduced risk of developing low bone mineral density	

Table definitions:

Population: The target population for the pharmaceutical, including any population defining characteristics (eg line of therapy, disease subgroup)

Intervention: Details of the intervention pharmaceutical (dose, frequency, treatment duration/conditions for treatment cessation).

Comparator: Details the therapy(s) that the target population would receive currently (status quo – including best supportive care; dose, frequency, treatment duration/conditions for treatment cessation).

Outcomes: Details the key therapeutic outcome(s), including therapeutic intent, outcome definitions, timeframes to achieve outcome(s), and source of outcome data.

11. Oral feed 1.5kcal/mL – Exclusive enteral nutrition, adults with Crohn's disease

Application

11.1. The Advisory Committee reviewed the application for oral feed 1.5 kcal/mL for exclusive enteral nutrition (EEN) for the treatment of Crohn's disease (CD) in adults.

11.2. The Advisory Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

Reccomendation

11.3. The Advisory Committee **recommended** that access of oral feed 1.5 kcal/mL be widened to adults with Crohn's disease for use as exclusive enteral nutrition with a **high priority** within the context of treatment with special foods, subject to the following endorsement (deletions in ~~strikethrough~~):

> Higher subsidy by endorsement – Additional subsidy by endorsement is available for patients being bolus fed through a feeding tube, who have severe epidermolysis bullosa, or as exclusive enteral nutrition ~~in children under the age of 18 years~~ for the treatment of Crohn's disease, or for patients with COPD and hypercapnia, defined as CO_2 value exceeding 55mmHg. The prescription must be endorsed accordingly.

11.4. The Advisory Committee considered the following in making this recommendation:

- Adherence is important for effective treatment
- Adherence is most influenced by individual preference for the feed used for the EEN
- Polymeric feed is most palatable of the currently available, fully funded options
- There is less evidence supporting this the use of EEN for the treatment of CD in adults compared to children

Discussion

Māori impact

11.5. The Committee discussed the impact of funding oral feed 1.5kcal/ml for the use as EEN for treatment of CD on Māori health areas of focus and Māori health outcomes. The Committee noted that the prevalence of CD in Māori was lower than in non-Māori and that the incidence in Māori is likely to be low, with some evidence indicating that rates may be increasing (Qui et al. J Crohns Colitis. 2022;16: i590–i591). The Committee considered that EEN may be used peri-operatively with improved outcomes from surgery or avoidance of surgery achieved. The Committee noted that complications from any surgery occur more frequently in Māori (Perioperative Mortality in New Zealand Report. Health Quality & Safety Commission. 2019).

Impact on Pacific peoples, disabled people, tāngata whaikaha Māori, and other people who have been underserved by the health system

11.6. The Committee discussed the impact of funding EEN for adults with CD on Pacific, disabled, and underserved populations. The Committee considered that there will be little impact on these populations due to the small numbers of people expected to use this treatment. EEN does however provide another treatment option for these people.

Background

11.7. The Committee noted that the Special Foods Subcommittee had previously recommended that oral feed 1.5kcal/ml liquids were funded for people under 18 years for use in EEN in December 2013. The Committee noted that these people have funded access oral feed liquids since January 2016 via Special Authority and endorsement.

Health need

11.8. The Committee noted that CD is an inflammatory condition that affects the gastrointestinal tract from the mouth to the anus and that associated signs and symptoms depend on the site involved and the presentation of the disease (inflammatory, stricturing or penetrating). The Committee noted this condition was relapsing and remitting in nature.

11.9. The Committee noted that the reported incidence of CD in New Zealand varies from 16 per 100,000 people (Gearry et al. Inflamm Bowel Dis 2006; 12: 936-43) to 26.4 per 100,000 people (Su et al. Inflamm Bowel Dis 2016;22: 2238-44). The Committee considered that the mean age of a CD diagnosis is 27 years (range of 15 to 32 years is common). The Committee considered that the prevalence of CD of 155.2 per 100,000 (Gearry et al. Inflamm Bowel Dis 2006; 12: 936-43).

11.10. The Committee noted that the prevalence of CD in Māori was reported to be 23.9 per 100,000 people, as based on a Canterbury study (Gearry et al. Inflamm Bowel Dis 2006; 12: 936-43). The Committee noted that the prevalence reported in a Waikato study was reported to be 61.4 per 100,000 people, but noted that there were small case numbers to inform this (Seleq et al. Internal Medicine Journal. 2023: 1-6). The Committee noted that the incidence in Māori is likely to be low, with some evidence indicating that rates may be increasing (Qui et al. J Crohns Colitis. 2022;16: i590–i591). The Committee also noted that complications from any surgery occur more frequently in Māori (Perioperative Mortality in New Zealand Report. Health Quality & Safety Commission. 2019).

11.11. The Committee noted that standard treatment for adults with CD usually includes corticosteroids to control initial acute disease, administered with, or without, conventional immunomodulators to reduce the risk of relapse. The Committee considered if treatment is ineffective then TNF inhibitors or other biologic drugs are administered, followed by surgery.

11.12. The Committee considered that EEN is the first line of therapy for uncomplicated, mild to moderate CD in children. The Committee considered that EEN is likely equivalent to oral corticosteroids in induction of remission of disease in this setting. The Committee noted that in children there is a greater desire to avoid corticosteroids due to the concern about growth impairment, however this is not a concern in adults. The Committee noted that of the children diagnosed with CD, 60% are malnourished at the time of diagnosis. The Committee considered that malnourishment at time of diagnosis in adults is much lower (reported as 16% (Pulley et al. JGH Open. 2019;4:454-60).

11.13. The Committee noted that people with inflammatory bowel disease (IBD) are eligible under Special Authority for full funding of oral feed powder and partial funding of the oral feed 1.5kcal/ml liquids.

11.14. The Committee noted that elemental and semi-elemental formulas (0.8-1.5 kcal/ml) are also fully funded on Special Authority and could be used by people with IBD for EEN.

Health benefit

11.15. The Committee considered that EEN provides all the required daily macro and micronutrients and can be used by people with IBD to reduce inflammation, provide a bridge to pharmacological treatment, assist with the management of fistula or abscess. The Committee considered that EEN was historically prescribed as either an elemental formula (amino acid based), semi-elemental formula (oligopeptide) formula or polymeric formula (oligopeptide or whole protein) which is now the preferred option. The Committee noted that oral elemental formula is currently the only option for vegan or milk allergic EEN patients. The Committee considered that

the semi-elemental or polymeric formulations are more palatable. The Committee considered that for an adult who is not malnourished a 30 kcal/kg dose is appropriate. The Committee noted that oral feed 1.5kcal/ml liquid is currently available in 200 to 237mL bottles, equivalent to 300 to 318 kcal per bottle. The Committee considered that the duration of treatment varies depending on the intention of treatment:

11.15.1. Induction of remission would be 6 to 8 weeks as a standard but up to 12 weeks if needed and tolerated.

11.15.2. A bridge for pharmacological treatment would be 4 to 12 weeks.

11.15.3. Preoperative exclusive enteral nutrition would be a minimum of 4 weeks.

11.15.4. Management of fistula or abscess would be 6 to 12 weeks.

11.16. The Committee noted a Cochrane review assessing the evidence for using EEN in people with CD for the induction of remission as a bridge to pharmacological therapy (Narula et al. Cochrane Database of Systematic Reviews. 2018 (4)). The Committee noted that the meta-analysis included eight randomised control trials with 223 participants. The Committee noted that the quality of the RCTs included in the meta-analysis was very low as indicated by the authors. The Committee noted that for adults, remission was 45% in the enteral nutrition group and 73% in the corticosteroid group (risk ratio (RR) 0.77, 95% CI, 0.58 to 1.03). The Committee noted that the withdrawal due to adverse events (169 participants) was 23% in the enteral nutrition group compared to 6% in the corticosteroid group (RR 2.95, 95% CI, 1.02 to 8.48).

11.17. The Committee noted a prospective, non-randomised, pilot study with 38 participants, conducted in New Zealand assessing enteral nutrition (EEN for two weeks followed by EEN or partial enteral nutrition (PEN) for six weeks) (Wall et al. Inflamm Intest Dis. 2018;2(4):219-27). The Committee noted that at week two 25 participants were still adhering to the EEN and at week six 14 participants were still using either PEN or EEN. The Committee noted a reported increase in people with faecal calprotectin less than 500ng (29% at week 0 v 36% at week 8). The Committee considered these reported results are uncertain clinical relevance as normal faecal calprotectin is less than 200-300ng. The Committee noted that for people that adhered to the dietary intervention (EEN or PEN) there was a decrease in BMI.

11.18. The Committee noted an observational study in people with fistulas/abscesses (*n*=33) or strictures (*n*=10) prescribed 12 weeks of EEN (Yang et al. Scand J Gastroenterol. 2017; 52(9): 995-1001). The Committee noted the reported results from the study including full remission in 60% of participants; partial remission in 20% of participants; abscess resolution in 76% of participants; CDAI decreased (223 initially and 106 at study conclusion, *P*<0.001); closure of entero-cutaneous fistula in 75% of participants and, resolution of stenosis in 20% of participants. The Committee considered that resolution of abscesses was a meaningful clinical beneficial but noted the small size of the study.

11.19. The Committee noted a prospective observational study with 59 participants with inflammatory bowel stricture (Hu et al. J Clin Gastroenterol. 2014; 48(9):790-5). The Committee noted that 50 participants completed the study and clinical remission was experienced by 42 participants.

11.20. The Committee noted a systemic review of people with fibrostenotic CD, including three studies (one retrospective and two prospective) using EEN (Cooper et al. Front Nutr. 2023; 10:1017382).

11.21. The Committee noted a retrospective case-control study with 51 participants (matched 1:2) with CD who were undergoing surgery for strictures or penetrating complications of the disease who received EEN pre-operative conditioning, or usual care for matched controls (Heerasing et al. Aliment Pharmacol Ther. 2017; 45:660-9). The Committee noted that the 25% of participants avoided surgery and post-operative complications were seen in 20% in the control group and only 3% in the EEN group. The Committee noted a systemic review of people undergoing surgery for CD including four studies (Rocha et al. GE Port J Gastroenterol. 2019; 26(3):184-195). The Committee noted that for people using EEN there was a decreased rate of anastomotic breakdown, abscess, wound infections and ileus reoperations. The Committee noted a systemic review of people using pre-operative EEN on nutritional and clinical outcomes of participants undergoing surgery (Gordon-Dixon et al. Clin Nutr ESPEN. 2021; 46:99-105). The Committee noted that the infectious complications decrease and there is a reported trend of decreased stoma formation. The Committee considered that there may be benefit in enteral nutrition (EEN or PEN) pre-operatively for post-operative outcomes.

11.22. The Committee noted the following additional studies:

- Wall et al. World J Gastroenterol. 2013; 19(43):7652-60
- Kakkadasam et al. J Crohns Colitis. 2020;14:S505 (abstract only)
- Shukla et al. J Crohns Colitis. 2019;14:S041 (abstract only)
- Guo et al. Nutr Clin Pract. 2013; 28(4):499-505
- Griffiths et al. Gastroenterology. 1995; 108(4):1056-67
- Di Caro et al. Nutrients. 2019;11:2222

11.23. The Committee considered that in New Zealand EEN is rarely used in adults, as there is much less evidence to support its use and palatability issues are more prevalent.

11.24. The Committee noted that EEN in adults is not routinely recommended to induce remission of Crohn's Disease in New Zealand. The Committee noted that EEN is not indicated for maintenance of remission ongoing. The Committee noted that there is no New Zealand guideline treatment for adults with CD and that the European Crohn's and Colitis Organisation (ECCO)/European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) 2014 does not discuss the use of EEN in adults. The Committee noted the following guidelines also did not discuss the use of EEN in CD in adults: Canadian Association of Gastroenterology; European Society of Parenteral and Enteral Nutrition 2017; Cochrane Systematic Review 2019; Croatian Guidelines 2010; North American Guidelines 2021 . The Committee noted that the Japanese guidelines from the guidelines research group 2021 did discuss EEN and that in Japan EEN is commonly used first line (Nakase et al. J Gastroenterol. 2021;56:489-526).

Suitability

11.25. The Committee considered that the evidence for the effect of individual preference on adherence was moderate strength and quality. The Committee noted that an Australia-New Zealand working group, proposed an optimal care pathway and considered five points that were important to improve adherence including: individual preference; availability and access to funded options; route of administration; convenience; and nutritional content (Day et al. JGH Open. 2020;4(2): 260-66). The Committee noted that the working group considered that the primary reason for high rates of nonadherence and withdrawal from trials amongst adults was the poor palatability of EEN.

11.26. The Committee noted a study that assessed palatability of elemental and polymeric formula via taste test in New Zealand. The Committee noted that the polymeric formula was preferred by 91% of participants and rated favourably compared with elemental formula for drinkability, flavour, mouth feel and acridity (*P*<0.001). The Committee noted that participants would consider treatment with exclusive enteral nutrition for eight weeks for 97% of participants for severe symptoms, 80% of participants for moderate symptoms and by 43% of participants for mild symptoms (Wall et al. e-SPEN Journal. 2014; 9:e200-e3). The Committee considered that those with mild disease were the most likely to benefit and be offered EEN in practice.

11.27. The Committee considered that it may be difficult for adults to adhere to this diet and unless the person has severe disease they are typically reluctant to try EEN as a treatment. The Committee noted that people receiving EEN would have increased adherence with dietitian support.

Cost and savings

11.28. The Committee considered that current treatment of adults consists of oral feed powder and corticosteroids, with elemental feed also being fully funded but infrequently used.

11.29. The Committee considered that the main benefit of this proposal was improved adherence to EEN with polymeric formula and a small reduction in the use of steroids. The Committee considered that the outcomes that should be included in the PICO include reduced need for surgery and post-operative complications (Heerasing et al. 2017; Rocha et al. 2019; Gordon Dixon et al. 2021). The Committee considered that measurement of post-operative complications was challenging. The Committee considered that there is some evidence indicating that the time to remission may be slower with EEN than with steroids.

11.30. The Committee considered that the uptake of EEN would be low. The Committee considered that each gastroenterologist would likely initiate two people per year on this treatment and estimated that nationally this would equate to around 200 people per year.

Funding criteria

11.31. The Committee considered that the age restriction could be removed in the endorsement criteria to allow use of EEN in adults.

Summary for assessment

11.32. The Advisory Committee considered that the table below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for oral feed 1.5 kcal/mL if it were to be funded in New Zealand for EEN for adults with CD. This PICO captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO is based on the Advisory Committee's assessment at this time and may differ from that requested by the applicant. The PICO may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

Population	Adults (aged 18 and over) with CD who require EEN for induction of remission of Crohn's disease or as a pre-operative conditioning for surgery for management of Crohn's disease
Intervention	Oral feed 1.5kcal/ml for 6-8 weeks. Dose is dependent on nutritional requirements and adjusted based on weight and height.

Comparator(s) (NZ context)	Oral feed powder Oral elemental feed 0.8 kcal/ml Corticosteroids
Outcome(s)	• Improved likelihood of adherence to treatment resulting in increased likelihood of induced remission and improved nutrition • Possible increased time in remission compared with corticosteroids • Reduced risk of steroid-related side-effects • Possible reduction in need for surgery • Possible reduction in post-operative complications

Table definitions:
Population: The target population for the pharmaceutical, including any population defining characteristics (eg line of therapy, disease subgroup)
Intervention: Details of the intervention pharmaceutical (dose, frequency, treatment duration/conditions for treatment cessation).
Comparator: Details the therapy(s) that the target population would receive currently (status quo – including best supportive care; dose, frequency, treatment duration/conditions for treatment cessation).
Outcomes: Details the key therapeutic outcome(s), including therapeutic intent, outcome definitions, timeframes to achieve outcome(s), and source of outcome data.

12. Oral feed liquid – amendment of criteria for people with COPD

Application

12.1. The Advisory Committee reviewed the application for oral feed 1.5 kcal/mL for people with COPD.

12.2. The Advisory Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

Recommendation

12.3. The Advisory Committee **recommended** that the current access criteria be amended with a high priority within the context of treatment with special foods, as follows (additions in **bold** and deletions in ~~strikethrough~~):

Special Authority
Initial application — (Long-term medical condition) from any relevant practitioner. Approvals valid without further renewal unless notified for applications meeting the following criteria:
Any of the following:

1. Is being fed via a tube or a tube is to be inserted for the purpose of feeding (not nasogastric tube - refer to specific medical condition criteria); or
2. Cystic Fibrosis; or
3. Liver disease; or
4. Chronic Renal failure; or
5. Inflammatory bowel disease; or
6. **Both:**
   - **6.1. Patient has** chronic obstructive pulmonary disease ~~with hypercapnia~~
   - **6.2. Any of the following:**
     - **6.2.1. Patient has a body mass index (BMI) of less than 18.5 kg/m2; or**
     - **6.2.2. Patient has unintentional weight loss greater than 10% within the last 3-6 months; or**
     - **6.2.3. Patient has a BMI of less than 20 kg/m2 and unintentional weight loss greater than 5% within the last 3-6 months)**; or
7. Short bowel syndrome; or
8. Bowel fistula; or
9. Severe chronic neurological conditions; or
10. Epidermolysis bullosa; or
11. AIDS (CD4 count < 200 cells/mm3); or
12. Chronic pancreatitis.

Higher subsidy by endorsement – Additional subsidy by endorsement is available for patients being bolus fed through a feeding tube, who have severe epidermolysis bullosa, or as exclusive enteral nutrition in children under the age of 18 years for the treatment of Crohn's disease, or for patients with COPD and **malnutrition (patient has a body mass index (BMI) of less than 18.5 kg/m2 OR unintentional weight loss greater than 10% within the last 3-6 months OR BMI of less than 20 kg/m2 and unintentional weight loss greater than 5% within the last 3-6 months)** ~~hypercapnia, defined as CO_2 value exceeding 55mmHg~~. The prescription must be endorsed accordingly.

12.4. The Advisory Committee considered the following in making this recommendation:

- COPD disproportionately affects Māori, Pacific peoples and people living in areas of highest deprivation (as measured by NZDep quintiles).
- For people with COPD it is more appropriate for oral feeds to be funded for people with malnutrition than restricting funding to those with hypercapnia.
- Some people cannot reconstitute the oral powder because it is too physically burdensome and therefore it is not used, or is not used at the concentration required to meet nutritional requirements.
- The liquid formulation has a higher energy density which may make it easier for people to meet their nutritional requirements.

Discussion

Māori impact

12.5. The Committee discussed the impact of funding oral feed 1.5kcal/mL for the treatment of malnutrition in COPD on Māori health areas of focus and Māori health outcomes. The Committee noted it was reported that the estimated age-standardised population prevalence for severe COPD was higher for Māori than for those of non-Māori, non-Pacific, and non-Asian ethnicity and for people of Asian ethnicity. The Committee noted that the average age of Māori with COPD were younger than those of non-Māori, non-Pacific or non-Asian ethnicity. The Committee noted the reported hospitalisation rates for Māori with COPD are 3.7 times the rate of people of non-Māori, non-Pacific and non-Asian (non-MPA) ethnicity. The Committee considered that Māori and people living in areas of highest deprivation (as measured by NZDep quintiles) are most impacted by COPD.

Impact on Pacific peoples, disabled people, tāngata whaikaha Māori, and other people who have been underserved by the health system

12.6. The Committee discussed the impact of funding liquid oral feeds for the treatment of malnutrition in COPD on Pacific, disabled, and underserved populations. The Committee noted it was reported that the estimated age-standardised population prevalence for severe COPD for Pacific peoples was higher than those of non-Māori, non-Pacific, and non-Asian (non-MPA) ethnicity and people of Asian ethnicity. The Committee noted that the average age of Pacific peoples and Asian peoples with COPD were younger on average than non-Māori, non-Pacific or non-Asian ethnicity. The Committee noted the reported hospitalisation rate for Pacific peoples with COPD is 2.8 times the rate of people of non-Māori, non-Pacific and non-Asian (non-MPA) ethnicity.

12.7. The Committee noted that for people living in areas of highest deprivation (as measured by NZDep quintiles) are 5.7 times more likely to be hospitalised with COPD.

12.8. The Committee considered that Māori, Pacific peoples and those living in low socioeconomic status are most impacted by COPD.

Background

12.9. The Committee noted that oral feed 1.5 kcal/mL liquids have been funded since March 2020 following the discontinuation of Pulmocare for people with COPD with hypercapnia. The Committee noted that Pulmocare was formulated with a high fat to protein ratio to reduce the production of carbon dioxide in people with COPD. The Committee noted previous advice considered that funded oral feed 1.5kcal/ml liquids were an appropriate alternative for Pulmocare for COPD with hypercapnia >55mmHg.

Health need

12.10. The Committee noted that COPD is a lung condition caused by the abnormalities of the airways that cause persistent, often progressive, airflow obstruction. The Committee noted that this progressive decline in lung function can be measured by forced expiratory volume (FEV1). The Committee noted that these obstructions often result in people with COPD not being able to breathe enough carbon dioxide out, causing physiological hypercapnia (high blood concentrations of carbon dioxide) resulting in a change in the person's breathing that causes them to feel out of breath.

12.11. The Committee considered that for people with COPD, malnutrition and weight loss develop as disease severity increases. The Committee considered that in people with severe COPD, weight loss, muscle mass loss and anorexia are common and are poor prognostic factors. The Committee considered that low BMI and low fat-free mass are associated with worse outcomes including impaired lung function, increased hospitalisations, poor exercise tolerance, worsened quality of life and increased mortality. The Committee considered that the estimated energy requirements to gain weight can increase from 25 kcal/kg to 45 kcal/kg.

12.12. The Committee noted a report from the Asthma and Respiratory Foundation New Zealand on the impact of respiratory disease in New Zealand 2020 (Barnard and Zhang, The impact of respiratory disease in New Zealand: 2020 update. 2021). The Committee noted it was reported that the estimated age-standardised population prevalence for severe COPD by ethnicity was as follows: Māori (2.50%); Pacific peoples (2.44%);non-Māori, non-Pacific, and non-Asian (non-MPA) ethnicity (0.83%); and Asian peoples (0.35%). The Committee noted that the average age of Māori with COPD was 61.3 years, compared with 62.6 for Pacific peoples, 65.7 for Asian peoples, and 70.7 for people of non-Māori non-Pacific or non-Asian ethnicity. The Committee noted the reported hospitalisation rates for Māori with COPD were 3.7 times the rate of people of non-Māori, non-Pacific and non-Asian (non-MPA) ethnicity. The Committee noted the reported hospitalisation rates for Pacific peoples with COPD were 2.8 times the rate of people of non-Māori, non-Pacific and non-Asian (non-MPA) ethnicity. The Committee noted that people living in areas of highest socioeconomic deprivation were 5.7 times more likely to be hospitalised with COPD. The Committee considered that Māori, Pacific peoples and those living in areas of socioeconomic deprivation are most impacted by COPD.

12.13. The Committee considered that there are other groups who may have similar health need to those with COPD and malnutrition that would benefit from oral feed liquids in particular children with inflammatory bowel disease who are malnourished. The Committee considered that fully funding oral feed 1.5 kcal/mL liquids for all people currently funded under Special Authority (ie removing the endorsement criteria) would remove this barrier and allow more choice for prescribers and the people they treat.

Health benefit

12.14. The Committee considered that people with COPD who are malnourished currently access full funding of oral feed powder and partial funding of oral feed liquid through both the COPD with hypercapnia criteria and the malnutrition criteria. The

Committee considered that people with COPD with and without hypercapnia are treated the same from a dietetic perspective. The Committee considered that there are no guidelines for the restriction of access to oral feed 1.5 kcal/mL liquids on the basis of hypercapnia and it is not current practice in New Zealand.

12.15. The Committee noted international guidelines and recommendations for nutritional support in people with COPD. The Committee noted the Global Initiative for Chronic Lung Disease (GOLD) recommended that in malnourished people with COPD nutrition supplements promote weight gain and improved respiratory muscle strength and overall health-related quality of life (Global Initiative for Chronic Obstructive Lung Disease (GOLD). 2023 Report).

12.16. The Committee noted the National Institute of Clinical Excellence (NICE) nutritional guidelines for people with COPD recommended that people with low BMI are given nutritional supplements to increase their total calorie intake and encourage exercise to increase muscle mass. The Committee noted that guidelines and recommendations were based on expert opinion and some small randomised clinical trials.

12.17. The Committee noted evidence to support the effect of nutritional supplements in people with COPD (Ferreira et al. Cochrane Database Syst Rev. 2012;12; Collins et al. Am J Clin Nutr. 2012;95: 1385-95; Collins et al. Respirology. 2013;18:616-29; Collins et al. J Thorac Dis. 2019;11(Suppl 17):S2230-7; Hoong et al. Clin Nutr. 2017;36:1105- 9; Bernardes et al. Br J Nutr. 2022:1-18). The Committee considered that overall, it was reported nutrition supplements improved fat mass, weight, hand-grip and made activities of daily living (ADL's) easier in malnourished people. The Committee considered that malnutrition increased healthcare use, reduced functional capacity, resulted in poorer clinical outcomes, and increased length of hospital stay. The Committee considered the evidence was moderate to low quality.

12.18. The Committee noted that comparators in the Randomised Control Trials (RCTs) are placebo, rather than directly comparing a liquid vs powder feed. The Committee considered that the benefit seen in the trials might be applicable to a proportion of the COPD with malnutrition population that were unable to, or preferred not to, use the powder feed. The Committee noted there is no evidence of a benefit for people who are already using oral powder feed.

12.19. The Committee considered that the measurement of hypercapnia is not readily available or frequently used in the diagnosis or prognosis of COPD. The Committee considered that this test is not accessible to dietitians as arterial blood gases are not routinely measured in the community. The Committee considered that there was no clear association between reducing carbon dioxide production through diet and clinical outcomes, however it might help identify people with COPD at risk of poor outcomes.

Suitability

12.20. The Committee considered that the currently funded option of oral feed powder requires reconstituting by adding 6 scoops (1kcal/mL) or 9 scoops (1.5kcal/mL) to 195mL of water mixing and then consuming. The Committee noted that for the final reconstituted product 6 scoops is equivalent to 230kcal, while 9 scoops is equivalent to 345kcal. The Committee considered that most dietitians would consider nine scoops to be more appropriate dosing, which is closer to the liquid formula, at 300kcal per 200mL serve. The Committee considered that while nine scoops increases the concentration of the final drink, this makes it the final product grittier and less palatable for people to drink. The Committee considered that this decreased people's adherence and therefore the benefit they would receive from

nutritional supplementation. The Committee considered that the powder can be added to other liquids or food products which can be beneficial in some situations.

12.21. The Committee considered that GPs would be more likely to prescribe six scoops, and that for the group overall, the dosing split may be about 40% prescribed six scoops, and 60% prescribed nine scoops.

12.22. The Committee noted that the oral feed 1.5kcal/mL liquids did not require reconstitution and are at a higher energy density already. The Committee considered that the oral feed 1.5 kcal/mL liquid is more palatable, and does not require physical effort to prepare, making it more suitable for people with COPD. The Committee considered that for people who cannot reconstitute the oral powder because it is too physically burdensome this responsibility often falls to a family member or caregiver.

Cost and savings

12.23. The Committee considered that the appropriate comparator for this proposal was nine scoops (81 g) of the oral feed powder reconstituted to 230 mL (Ensure powder) twice daily or six scoops (56 g) reconstituted and taken three times daily. The Committee considered that people are using more of the powder than estimated using the standard 1 kcal/mL twice daily instructions.

12.24. The Committee considered that approximately 20% of people with COPD have weight loss, and protein and calorie malnutrition. The Committee considered that currently, approximately 10,000 people access oral feed (powder or liquid with a part charge) through the malnutrition criteria but noted that this would include many people with indications other than COPD. The Committee considered that the number of people who would be eligible for access to oral feed 1.5 kcal/mL liquids if this proposal was funded would therefore be less than 10,000, however considered the exact number to be highly uncertain. The Committee considered that a population study of malnutrition with a breakdown by indication may shed light on the proportion of people accessing oral feed for malnutrition that may have COPD.

12.25. The Committee considered that 70% of people with COPD with hypercapnia are accessing the oral feed powder as a fully funded option and only 30% are accessing fully funded liquids via the endorsement criteria. The Committee noted that many clinicians prescribing through the COPD with hypercapnia criteria would be unaware of the endorsement, therefore considered it unlikely many eligible people are getting the fully funded liquid.

12.26. The Committee considered that those that do not have hypercapnia are able to access oral feeds through the malnutrition criteria. The Committee considered it reasonable to assume the breakdown would be the same amongst people with COPD accessing oral feeds via the malnutrition criteria when considering fully funded powder (70% of people) compared to partially funded liquid (30% of people).

12.27. The Committee considered that if access to oral feed 1.5 kcal/mL liquids were amended to include people with COPD with malnutrition, uptake of the liquid would be high and that approximately 80% of patients currently using the oral feed powder 1kcal/mL would switch to the ready to drink liquid (1.5kcal/mL), based on professional experience. The Committee noted that there is no evidence to support a reduction in number of hospitalisations or length of stay in hospital as a result of using oral feed 1.5 kcal/mL liquids compared with the status quo, however considered that the improved ease of ADL's is likely to translate to a health-related quality of life benefit.

Funding criteria

12.28. The Committee considered that modifying the Special Authority criteria to include malnutrition rather than hypercapnia would be unlikely to change uptake to currently funded treatments for people with COPD. The Committee considered that for those that did not meet the COPD with hypercapnia criterion, would meet the malnutrition criteria for funding. The Committee noted that the malnutrition criteria did not include a break down by indication.

12.29. The Committee considered that modifying the endorsement criteria to include COPD with malnutrition would enable people with COPD fully funded access to the oral feed 1.5 kcal/mL liquid presentation.

12.30. The Committee considered that the definition of malnutrition as described in the Special Authority for malnutrition was appropriate (person has a body mass index (BMI) of less than 18.5 kg/m^2; or person has unintentional weight loss greater than 10% within the last 3-6 months, OR a BMI of less than 20 kg/m^2 and unintentional weight loss greater than 5% within the last 3-6 months).

12.31. The Committee considered that primary care practitioners may not be aware of the current endorsement criteria that may provide access to fully funded oral feed 1.5 kcal/mL liquids for some of the people in their care and this was an existing barrier for people with COPD.

Summary for assessment

12.32. The Advisory Committee considered that the table below summarises its interpretation of the most appropriate PICO (population, intervention, comparator, outcomes) information for oral feeds 1.5 kcal/mL if it were to be funded in New Zealand for malnutrition. This PICO captures key clinical aspects of the proposal and may be used to frame any future economic assessment by Pharmac staff. This PICO is based on the Advisory Committee's assessment at this time and may differ from that requested by the applicant. The PICO may change based on new information, additional clinical advice, or further analysis by Pharmac staff.

Population	People with COPD who are malnourished
Intervention	Oral feed 1.5 kcal/mL, in 200mL serves. Twice per day on average
Comparator(s) (NZ context)	Oral feed powder, two serves of 81 g per day, made up into a 230mL solution OR Oral feed powder, three serves of 56 g per day, made into a 230 mL solution. Some individuals may be choosing to part fund the oral feed 1.5kcal/mL
Outcome(s)	Weight stability, improved hand grip and improved ease of ADL's which are likely to translate to an improved quality of life.

Table definitions:
Population: The target population for the pharmaceutical, including any population defining characteristics (eg line of therapy, disease subgroup)
Intervention: Details of the intervention pharmaceutical (dose, frequency, treatment duration/conditions for treatment cessation).
Comparator: Details the therapy(s) that the target population would receive currently (status quo – including best supportive care; dose, frequency, treatment duration/conditions for treatment cessation).
Outcomes: Details the key therapeutic outcome(s), including therapeutic intent, outcome definitions, timeframes to achieve outcome(s), and source of outcome data.