

**5.18 AMINO ACID FORMULA WITH CARBOHYDRATE,
VITAMINS, MINERALS AND TRACE ELEMENTS
WITHOUT PHENYLALANINE, SUPPLEMENTED WITH
DOCOSAHEXAENOIC ACID**

**Sachets containing oral powder 33 g, 30 (PKU
Synergy),**

PKU Synergy[®], Nutricia Australia Pty Ltd

1 Purpose of Application

- 1.1 The minor submission requested an Authority Required listing of PKU Synergy[®] for the dietary management of Phenylketonuria (PKU) or hyperphenylalaninaemia in children from 10 years of age or adults.

2 Requested Listing

- 2.1 The submission requested the following new listing:
- 2.2 The Secretariat noted that patients with hyperphenylalaninaemia are not a separate population and are captured by the indication for PKU.

Public Summary Document – July 2017 PBAC Meeting

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Manufacturer	Name and
AMINO ACID FORMULA WITH CARBOHYDRATE, VITAMINS, MINERALS AND TRACE ELEMENTS WITHOUT PHENYLALANINE, SUPPLEMENTED WITH DOCOSAHEXAENOIC ACID oral liquid: powder for, 30 x 33 g sachets	2	5	\$979.24	PKU Synergy®	Nutricia Australia Pty Ltd

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
PBS Indication:	Phenylketonuria
Restriction Level / Method:	<input checked="" type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined

3 Background

- 3.1 The sponsor of PKU Synergy® claimed that it meets the requirements for foods that have medical purposes as set out under *The Australia New Zealand Food Standards Code – Standard 2.9.5: Food for Special Medical Purposes*.
- 3.2 The minor submission claimed that PKU Synergy® is nutritionally incomplete and is intended to be used as a supplement.
- 3.3 PKU Synergy® contains magnesium and calcium at levels that exceed the upper limit of the recommended daily intake for some patients. The sponsor claimed that dietary intake of these nutrients would be limited in patients with phenylketonuria and therefore the higher levels of these nutrients were of no nutritional concern.
- 3.4 PKU Synergy® has not been considered by PBAC previously.

4 Comparator

- 4.1 The minor submission nominated PKU Express 20® and Lophlex® as the main comparators. All three products contain 20 g protein equivalent (PE) per sachet and are all powdered protein substitutes.

- 4.2 It was noted that PKU Synergy® contains 4.3 mg of phenylalanine per sachet, whereas the main comparators PKU Express 20® and Lophlex® are phenylalanine free.

For more detail on PBAC’s view, see section 6 “PBAC outcome.”

5 Consideration of the evidence

Sponsor hearing

- 5.1 There was no hearing for this item as it was a minor submission.

Consumer comments

- 5.2 The PBAC noted that no consumer comments were received for this item.

Clinical trials

- 5.3 As a minor submission, no clinical trials were presented in the submission.
- 5.4 In consideration of the submission, the Nutritional Products Working Party (NPWP) noted that:
- The sponsor did not provide a suitable comparison against the requirements of the Australia New Zealand Food Standards Code - Standard 2.9.5: Food for Special Medical Purposes. The NPWP also noted that the relevant comparison is per serve – the product is only 1 serve per day and the comparators 3-4 serves per day (if compliant).
 - The product does not contain copper and only extremely low levels of phosphorus both of which are essential elements.
 - The product actually contains lower levels of vitamin B6, folate, biotin and niacin than comparators.
 - There were higher levels of only some vitamins in the formulation compared to the comparators PKU Express 20® and Lophlex®. The NPWP questioned whether there would be any additional benefits, because patients with phenylketonuria do not typically present with vitamin deficiencies if compliant with supplements.
 - There was a lack of clinical data to indicate a clinical need for the product to support this application.

The NPWP did not support the request to list PKU Synergy® for the dietary management of phenylketonuria. The NPWP considered there was no clinical need for the requested listing, noting that the formula does not contain copper or adequate levels of phosphorus, contains higher levels of only some vitamins compared with the comparators, and that there were no obvious additional benefits. Further, the NPWP considered the recommendation to restrict the proposed treatment to one sachet a day is potentially confusing for consumers as this is different from what is currently recommended for other amino acids supplements.

Estimated PBS usage & financial implications

- 5.5 The minor submission claimed that PKU Synergy® will be essentially cost neutral to the PBS as PKU Synergy® is priced per PE at the same price as PKU Express 20® and Lophlex® of \$0.81 per gram PE (calculated based on the DPMQ). The proposed DPMQ for PKU Synergy® is \$979.24.
- 5.6 The minor submission claimed that the volume and proportion of usage will be small in terms of patient numbers as the introduction of PKU Synergy® into the Australian market will not result in any new patients commencing dietary therapy.
- 5.7 The minor submission estimated that approximately █% (n=█) of patients currently taking PKU Express 20® or Lophlex® would be non-compliant in their dietary therapy and will therefore switch to PKU Synergy®. The minor submission presented this estimate (n=█) as the maximum number of patients that would be expected to convert to PKU Synergy® in the first five years of listing.
- 5.8 The minor submission estimated a net cost to the PBS of substantially less than \$10 million over the first 5 years of listing, due to the requirement for an additional number of scripts required per year compared to the main comparators.
- 5.9 The minor submission claimed that PKU synergy® will improve compliance in PKU patients with a higher phenylalanine tolerance, therefore potentially reducing product wastage resulting in savings to the PBS.

For more detail on PBAC's view, see section 6 "PBAC outcome."

6 PBAC Outcome

- 6.1 The PBAC decided to defer its decision on whether to recommend the listing of amino acid formula with carbohydrate, vitamins, minerals and trace elements without phenylalanine, supplemented with docosahexaenoic acid; for the dietary management of PKU. The PBAC considered that there was a lack of clinical data to indicate a clinical need for the product but noted the pre-PBAC response from the

sponsor and considered that these responses should be considered by the NPWP before finalising its decision.

- 6.2 The PBAC noted that the requested listing also included patients with hyperphenylalaninaemia; however, the PBAC noted that these patients were not a separate patient population from the PKU patient population.
- 6.3 The PBAC noted the advice of the Nutritional Products Working Party (NPWP) that supported the decision to not recommend listing the product on the PBS.
- 6.4 The PBAC noted that the product does not contain copper and only extremely low levels of phosphorus that are essential elements, and also lower levels of Vitamin B6 folate, biotin and niacin than its comparators, PKU Express 20® and Lophlex®.
- 6.5 The PBAC considered the recommendation to restrict the proposed treatment to one sachet a day would be potentially confusing for consumers as this is different from what is currently recommended for other amino acids supplements in this indication.
- 6.6 The PBAC noted the pre-PBAC response from the sponsor and considered that input from the NPWP was required to assess whether the response adequately justified their claims.
- 6.7 The PBAC noted the NPWP's advice that there was no clinical need for the requested listing.
- 6.8 The PBAC noted that this submission is not eligible for an Independent Review as it has been deferred for further discussion.

Outcome:

Deferred

7 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

8 Sponsor's Comment

The sponsor had no comment.

November 2017 addendum to the July 2017 PBAC Minutes:

4.01 AMINO ACID FORMULA WITH CARBOHYDRATE, VITAMINS, MINERALS AND TRACE ELEMENTS WITHOUT PHENYLALANINE, SUPPLEMENTED WITH DOCOSAHEXAENOIC ACID Sachets containing oral powder 33 g, 30 (PKU Synergy®), PKU Synergy®, Nutricia Australia Pty Ltd

9 Background

9.1 At the July 2017 PBAC meeting, the PBAC noted the Nutritional Products Working Party (NPWP) advice and considered there was a lack of clinical data to indicate a clinical need for PKU Synergy®, noting that the formula does not contain copper or adequate levels of phosphorus, contains higher levels of only some vitamins compared with the comparators, and that there were no obvious additional benefits. However, the committee noted the pre-PBAC response from the sponsor and decided to defer their decision on PKU Synergy® to allow for consideration of the pre-PBAC response by the NPWP.

10 Consideration of the evidence

10.1 In consideration of the July 2017 pre-PBAC response,:

- The NPWP noted that the sponsor claimed that the intended population for PKU Synergy® is adolescent and adult PKU patients with relatively 'relaxed diets' with higher phenylalanine tolerance, and an increase in protein intake, which negated the need for copper and phosphorus in PKU Synergy®. The sponsor also stated that the one dose per day was appropriate for the intended patient population based on its use under medical supervision.
- The NPWP noted that the pre-PBAC response did not provide any new clinical evidence to support the claim. The NPWP remained unconvinced that use of the product would provide enough copper and phosphorus for patients on a relaxed diet and considered that if the diets were sufficiently relaxed to meet requirements for these nutrients, that there was no need for this product.

- The NPWP remained concerned with the proposed dosing regimen of one sachet per day and reiterated that this dosing regimen would be confusing and possibly detrimental to patients with PKU. The NPWP considered that there were other products with better nutritional profiles for this patient population and that there was no clinical need for the listing of PKU Synergy®.
 - The NPWP rejected the referred submission on the basis of the remaining significant concerns in regards to the nutritional profile in PKU Synergy®, which could be potentially harmful to patients with PKU.
- 10.2 The PBAC noted that the NPWP did not support the request to list PKU Synergy® for the dietary management of PKU.

11 PBAC Outcome

- 11.1 The PBAC did not recommend the listing of PKU Synergy® for the dietary management of phenylketonuria (PKU) or hyperphenylalanaemia in children from 10 years of age on the basis that the PBAC considered that there were other products with better nutritional profiles for this patient population. The PBAC advised that there was no clinical need for listing this product.
- 11.2 The PBAC noted that the pre-PBAC response for the November meeting has provided additional information to justify the rationale behind the requested listing. This information included anecdotal support from the sponsor's advisory board (which consisted of six metabolic dietitians from Australia and New Zealand). However, the sponsor did not provide any new clinical evidence to support its requested listing.
- 11.3 The PBAC noted the advice of the Nutritional Products Working Party (NPWP) to not recommend listing the product on the PBS.
- 11.4 The PBAC also noted the NPWP's advice that it remained unconvinced that use of the product would provide enough copper and phosphorus for patients on a relaxed diet and considered that if the diets were sufficiently relaxed to meet requirements for these nutrients, that there was no clinical need for PKU Synergy®.
- 11.5 The PBAC noted that this submission is eligible for an Independent Review.

Outcome:

Rejected

12 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final

PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

13 Sponsor's Comment

Whilst Nutricia is disappointed in the PBAC outcome, we will continue to work with the PBAC on demonstrating the value of PKU Synergy. Nutricia firmly believes that medical nutrition products are important in the nutritional management of patients with a disease, disorder or medical condition and will continue to seek subsidised access for patients.