

5.19 AMINO ACID FORMULA WITH VITAMINS, MINERALS AND LONG CHAIN POLYUNSATURATED FATTY ACIDS WITHOUT PHENYLALANINE, 10g Protein Oral liquid, 500 mL bottle, 20; PKU BABY; Orpharma Pty Ltd.

1 Purpose of Application

1.1 The minor submission requested a restricted benefit listing for phenylketonuria

2 Requested listing

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 VITAMINS, MINERALS AND LONG CHAIN POLYUNSATURATED FATTY ACIDS WITHOUT PHENYLALANINE Amino acid formula with vitamins, minerals and long chain fatty acids without phenylalanine containing 10 g protein, oral liquid, 500 mL bottle, 20	1	5	\$ [REDACTED]	PKU Baby	To be confirmed

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
Condition:	Phenylketonuria
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 PKU baby does not require registration with the TGA. The sponsor has confirmed 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 PKU Baby has not been considered by the PBAC previously.

4 Comparator

- 4.1 The submission nominates PKU Anamix Infant as the main comparator. PKU Baby and PKU Anamix Infant both are taken as oral liquids and both products contain 2g of protein equivalent per 100mL of liquid. However, PKU Anamix Infant requires reconstitution prior to use.

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.

Consideration of the evidence

Table 1: Clinical comparison of PKU Baby and powdered amino acid formulas (Stroem, Enggaard et al. 2011)

Citation	Stroem, P., Enggaard, K., et al. (2011). "When will PKU infants blood phenylalanine reach the desired level? - a study of 207 PKU patients." J Inherit Metab Dis 34(Suppl 3): S101. <i>The sponsor does not provide full details of the clinical study and the attachment 7 is a conference abstract</i>
Objective	To determine if there is a time difference as to when infants blood phe reached the desired level, depending on which phenylalanine free infant formula was used.
Formulas used	Liquid formula: PKU Baby Powdered formulas: PKU Anamix Infant (Nutricia), XPhé (MetaX), 2 other powder formulas that are no longer marketed in Denmark. (Source: Direct communication with Kennedy Centre authors).
Patients	207 PKU patients treated from birth at the Kennedy Centre, Denmark
Methods	PKU infants were divided into 3 groups according to phenotype – classical, moderate, and mild. Five different formulas – 1 liquid (PKU Baby), 4 powdered – were administered to the 3 patient groups. Number of days from start of treatment to blood phe reaching the desired level below

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	300 µmol/L (until year 2000 420 µmol/L) was recorded.
Results	Median number of days to reach desired blood phe level: Classical (N=115): Liquid 6 days vs. powdered 8-18 days. Moderate (N=11): Liquid (-) days vs. powdered 5-12 days. Mild (N=80): Liquid 4 days vs. powdered 5-8 days.

Source: table B.1-1 of the submission, page 21

- 5.3 The clinical trial, reported as a conference abstract, compared the use of PKU Baby and 4 other amino acid powder formulations, including the comparator PKU Anamix Infant. An overview of the clinical study and the results is provided in the table above.
- 5.4 The submission claimed that the study demonstrated that the PKU Baby liquid formula seems to be more efficient than the powdered formulas in reaching the desired blood phenylalanine level (below 300 µmol/L).
- 5.5 The submission states that therapeutic conclusion is that PKU Baby is equivalent or potentially superior to the comparator PKU Anamix Infant. As a minor submission, the clinical evidence was not evaluated.
- 5.6 In consideration of the submission, the Nutritional Products Working Party (NPWP) noted:
- The comparator PKU Anamix Infant® is appropriate, and has a similar amino acid composition to PKU Baby®. Although there are some differences to the vitamin and mineral profiles (such as iron), the clinical impact is uncertain.
 - The sponsor requested a price premium per gram of protein. The NPWP noted the reasons for the request for a price premium but considered that there was no additional benefit expected from this product compared to the currently listed alternatives. Although the submission claimed that phenylalanine levels in the study participants normalised swiftly, there was no evidence to suggest that this would significantly alter patient outcomes. The NPWP was concerned that the clinical claim in the submission may not be supported by the evidence provided. The non-peer-reviewed abstract contained no information about the initial phenylalanine levels of participants, the number of patients on liquid versus powder, no randomisation of participants, and no presentation of standard errors. Overall, the NPWP viewed that in practice this product would likely provide the same health benefit to patients as the alternatives listed on the PBS.
 - The sponsor claimed that this liquid product would result in less wastage than a powder product. The NPWP disagreed with this claim, noting that in clinical practice, patients are usually advised to use all prescribed product before switching products, or any excess cans for powders are used by other patients in the clinic.
 - Following the above considerations, listing this product on the equivalent price per gram of protein as per the comparator, PKU Anamix Infant® was appropriate.
 - The sponsor underestimated the quantity of this product required by an infant. Specifically, the sponsor estimated that 6 months' supply would provide

280mL/day (500mL x 20 x 5/180 days). However, infants are more likely to require 400-500mL (280-350 calories) per day, even considering supplemental breast/formula feeds and solids. Therefore, the NPWP considered the number of bottles (20) to be insufficient for a month’s supply, as recommended in the PBAC Guidelines.

- Although the sponsor stated that this product meets “Australia New Zealand Food Standards Code - Standard 2.9.5 - Food for Special Medical Purposes”, the NPWP noted that the submission, for a formula proposed to be used in infants younger than 12 months, did not provide a comparison with the requirements of the “Australia New Zealand Food Standards Code - Standard 2.9.1 - Infant Formula Products”, as recommended in the PBAC Guidelines.

5.7 The NPWP deferred its consideration of this submission until such time that clarification from the sponsor as to whether the product meets “Australia New Zealand Food Standards Code - Standard 2.9.1 - Infant Formula Products” can be sought.

5.8 The PBAC noted that the sponsor provided the requested information in its Pre-PBAC Response, however it was not possible in the available time for the NPWP to fully evaluate the information prior to the PBAC meeting.

Estimated PBS usage & financial implications

Table 2: Cost to the PBS of PKU Baby listing over the first 6 years.

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Total units*	█	█	█	█	█	█
Cost at DPMQ	\$█	\$█	\$█	\$█	\$█	\$█
Cost at DPMQ with average co-payment removed	\$█	\$█	\$█	\$█	\$█	\$█

Source table E.2-4 of the submission, page 26

* 1 unit = proposed PBS maximum quantity.

5.9 The submission requested a higher price per gram of protein compared with the comparator because █, clinical importance of an alternative PKU product for infants and the potential clinical advantages shown by PKU Baby in the clinical study. The DPMQ (\$█) requested in the submission represents an AEMP of \$█ per gram of protein content. The AEMP for PKU Amamix Infant is \$█ per gram of protein.

5.10 The submission assumes █ dispensing per year for this product. Though the product is expected to replace other PBS listed products for PKU, at the price requested, there is an additional cost to the PBS estimated to be \$█ in year 1 and \$█ in year 5.

6 PBAC Outcome

- 6.1 The PBAC deferred its recommendation until further advice could be provided by the NPWP on this submission in view of the additional information that was received from the sponsor.
- 6.2 The PBAC noted the price proposed in the submission and agreed with the NPWP that no additional health benefit had been demonstrated by this product compared to the currently listed alternatives.

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 thanks the PBAC for their considerations and looks forward to being able to list PKU Baby in the near future.