

5.25 AMINO ACID FORMULA WITH FAT, CARBOHYDRATE, VITAMINS AND MINERALS WITHOUT PHENYLALANINE, Tablets (modified release), 54 g protein per 100 g, 100 g, pack of 6 (PKU Easy Microtabs Plus) PKU Easy Microtabs Plus, ORPHARMA PTY LTD.

1 Purpose of Submission

- 1.1 The Category 3 submission requested a General Schedule Restricted Benefit listing of amino acid formula with fat, carbohydrate, vitamins and minerals without phenylalanine tablets (modified release), 54 g protein per 100 g, 100 g, pack of 6 (PKU Easy Microtabs Plus) for the dietary management of phenylketonuria (PKU). PKU Easy Microtabs Plus is a phenylalanine (phe)-free protein substitute in micro-tablet form with vitamins and minerals, intended for use in children aged 3 years and older, and adults with PKU requiring amino acid supplementation.
- 1.2 Listing was requested on the basis of cost-minimisation versus amino acid formula with fat, carbohydrate without phenylalanine tablets (modified release), 70.8 g protein per 100 g, 110 g, pack of 4 (PKU Easy Microtabs) at the same cost per gram of protein equivalent (PE).

2 Background

- 2.1 PKU Easy Microtabs Plus has not been previously considered by the PBAC.
- 2.2 The submission stated that PKU Easy Microtabs Plus meets the requirements for foods that have special medical purposes as set out under the *Australia New Zealand Food Standards Code – Standard 2.9.5: Food for Special Medical Purposes*.
- 2.3 As this product is marketed as a nutritional product, and not a therapeutic good, it is not registered in the Australian Register of Therapeutic Goods.

3 Requested listing

- 3.1 The submission requested the listing of PKU Easy Microtabs Plus under the same conditions as the current listing for PKU Easy Microtabs (PBS item code: 10683G).

Add new medicinal product as follows:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
AMINO ACID FORMULA WITH FAT, CARBOHYDRATE, VITAMINS AND MINERALS WITHOUT PHENYLALANINE					

amino acid formula with fat, carbohydrate, vitamins and minerals without phenylalanine tablet: modified release, 6 x100 g	NEW	7	7	5	PKU Easy Microtabs Plus
Restriction Summary [] / Treatment of Concept: []					
	Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners				
	Restriction type: <input checked="" type="checkbox"/> Restricted benefit				
	Indication: Phenylketonuria				

- 3.2 The submission requested a maximum quantity of 7 for PKU Easy Microtabs Plus, providing 2,268 g of PE content, slightly higher than the PE content in the currently listed PKU Easy Microtabs (2,181 g PE content per the maximum quantity of 7). The submission stated that this quantity meets the needs of all patient groups, including those with the highest daily protein requirements (e.g. 67 g/day for lactating women and 65 g for adolescent boys), and provides at least one month of therapy per prescription. The proposed 5 repeats would supply approximately 6 months of therapy, aligning with other phe-free amino acid nutritional products listed for PKU.

4 Comparator

- 4.1 The submission nominated the currently PBS-listed PKU Easy Microtabs as the main comparator. The submission indicated that PKU Easy Microtabs Plus would likely substitute for PKU Easy Microtabs if recommended for listing, as PKU Easy Microtabs is the most commonly used phe-free amino acid formula in tablet form for PKU on the PBS.
- 4.2 The submission noted that there are a number of phe-free amino acid formulae in different forms available on the PBS for PKU but did not nominate these as alternative comparators. Table 1 presents a list of phe-free amino acid formulae listed on the PBS for PKU.

Table 1: PBS-listed nutritional products for the dietary management of PKU

Medicinal Product	Form	Trade name	PBS item code	Max. qty packs	No. of Rpts
Amino acid formula with carbohydrate without phenylalanine	Tablets containing 0.92 g protein, 462	PKU Easy Tablet	12072J	4	5
Amino acid formula without phenylalanine	Tablets 1 g, 75	Phlexy-10	8678R	24	5
Amino acid formula with carbohydrate, vitamins, minerals and trace elements without phenylalanine	Sachets containing oral powder 20 g, 30	PKU Go	10806R	4	5
Amino acid formula with fat, carbohydrate, vitamins, minerals and trace elements without phenylalanine	Bottles containing oral powder 34 g, 30	PKU Easy Shake & Go	10632N	5	5
Amino acid formula with vitamins and minerals without phenylalanine	Oral liquid 62.5 mL, 60	PKU Lophlex LQ 10	9397N	2	5
	Oral liquid 87 mL, 30	PKU Cooler 10	2382J	4	5
	Oral liquid 125 mL, 30	PKU Lophlex LQ 20	9021T	4	5
	Oral liquid 125 mL, 36	PKU Anamix Junior LQ	9396M	4	5
	Oral liquid 125 mL, 30	PKU Lophlex Select LQ	14290D	4	5
	Oral liquid 130 mL, 30	PKU Cooler 15	8846N	4	5
	Oral liquid 174 mL, 30	PKU Air 20	10411Y	4	5
	Oral liquid 174 mL, 30	PKU Cooler 20	2474F	4	5
	Oral liquid 250 mL	Easiphen	8746H	90	5
	Oral gel 85 g, 30	PKU squeezeie	5483N	4	5
	Oral semi solid 109 g, 36	PKU Lophlex Sensation 20	2806Q	3	5
	Oral powder 500 g	XP Maxamum	2739E	8	5
	Sachets containing oral powder 25 g, 30	PKU express 15	8591E	4	5
	Sachets containing oral powder 28 g, 30	PKU Lophlex	12136R	4	5
	Sachets containing oral powder 34 g, 30	PKU express 20	1909L	4	5
Sachets containing oral powder 36 g, 30	PKU Anamix Junior	10258X	4	5	
Amino acid formula with vitamins, minerals and long chain polyunsaturated fatty acids without phenylalanine	Oral powder 400 g	PKU Anamix infant	8479G	8	5

Source: compiled by the Secretariat during the evaluation, using PBS restrictions for PBS-listed nutritional products as of August 2024, accessed on 1 September 2024.

Abbreviation: PBS = Pharmaceutical Benefits Scheme

4.3 PKU Easy Microtabs was recommended for the dietary management of PKU on a cost-minimisation basis compared to Phlexy-10 tablet at the same price per gram of protein (paragraph 6.1, PKU Easy Microtabs, Public Summary Document, November 2015 PBAC Meeting).

5 Consideration of the evidence

Sponsor hearing

5.1 There was no hearing for this item.

Consumer comments

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

Population and disease

5.3 PKU is a rare autosomal recessive metabolic disorder with an estimated incidence of approximately one in 10,000 live births in Australia (ASIEM¹, 2020). PKU is more common among Caucasians and affects both genders equally. Patients with PKU are born with a deficiency of the enzyme phenylalanine hydroxylase (PAH), which converts phe to tyrosine. Without treatment, elevated phe levels can cause severe intellectual and physical disabilities. The treatment includes a lifelong phe-restricted diet, with dietary therapy recommended for patients with a blood phe level above 360 µmol/L in Australia.

Nutritional profile

5.4 The nutrient content of PKU Easy Microtabs Plus and the main comparator, PKU Easy Microtabs, are presented in Table 2. The key difference between PKU Easy Microtabs Plus and PKU Easy Microtabs is that PKU Easy Microtabs Plus contains vitamins and minerals. The submission stated that PKU Easy Microtabs Plus will be the only phe-free amino acid formula in tablet form with vitamins and minerals on the PBS, if recommended for listing.

5.5 The submission stated that PKU Easy Microtabs Plus provides a substantial contribution to nutrient intake across all patient groups, including children, adolescents, men, women, and pregnant and lactating women. However, the submission noted that PKU Easy Microtabs Plus is not recommended as the sole source of nutrition and diet must be supplemented with natural protein, water and other nutrients in prescribed quantities to supply phenylalanine, fluid and general nutritional requirements.

Table 2: Nutrient content of PKU Easy Microtabs Plus and PKU Easy Microtabs

Nutrient and unit	PKU Easy Microtabs Plus (Per 100 g)	PKU Easy Microtabs (Per 100 g)
Protein (g)		
Energy, kJ	1428	1678
Fat, g	1.85	3.6

¹ ASIEM (2020). The PKU Handbook. Prepared by the Australasian Society for Inborn Errors of Metabolism (ASIEM). Accessed on 2 September 2024 at: <https://www.hgsa.org.au/common/Uploaded%20files/pdfs/asiem%20dietary%20handbooks/PKU.pdf>.

Public Summary Document – November 2024 PBAC Meeting

Nutrient and unit	PKU Easy Microtabs Plus (Per 100 g)	PKU Easy Microtabs (Per 100 g)
of which saturates, g	1.55	3.59
Protein, g	54	70.8
Carbohydrate, g	18	13
of which sugars, g	0.57	0.0
Fibre, g	17.1	3.7
Salt, g	1.32	1.0
Vitamins		
Vitamin A, µg	667	0
Vitamin D3, µg	8.4	0
Vitamin E, mg	7.5	0
Vitamin K, µg	58.3	0
Vitamin C, mg	41.7	0
Thiamin, mg	1.0	0
Niacin, mg	1.2	0
Vitamin B6, mg	16.7	0
Folic acid, µg	1.3	0
Vitamin B12, µg	585	0
Biotin, µg	20.8	0
Pantothenic acid, mg	4.2	0
Minerals		
Potassium, mg	161	0
Calcium, mg	667	0
Phosphorous	643	0
Magnesium	250	0
Iron	12.5	0
Zinc	9.2	0
Copper	1.25	0
Manganese	1.25	0
Selenium	63	0
Chromium	25.3	0
Molybdenum	58.3	0
Iodine	126	0
Amino acids		
L-Alanine, g	2.17	3.07
L-Arginine, g	3.46	4.9
L-Aspartate, g	5.49	7.76
L-Carnitine, g	0.057	0.08
L-Cystine, g	1.42	2.01
Glycine, g	5.43	7.68
L-Glutamine, g	4.26	6.02
L-Histidine, g	2.17	3.07
L-Isoleucine, g	3.75	5.31
L-Leucine, g	5.85	8.27
L-Lysine, g	3.89	5.5
L-Methionine, g	1.0	1.42
L-Proline, g	3.92	5.54
L-Serine, g	2.42	3.42
L-Threonine, g	3.75	5.31
L-Tryptophan, g	1.17	1.65
L-Tyrosine, g	5.50	7.78
L-Valine, g	4.34	6.13

Nutrient and unit	PKU Easy Microtabs Plus (Per 100 g)	PKU Easy Microtabs (Per 100 g)
Taurine, g	0.085	0.12

Source: Table 1-5 of the submission

Clinical trials

5.6 The submission did not provide any new clinical information specific to PKU Easy Microtabs Plus.

Clinical claim

5.7 The submission claimed that PKU Easy Microtabs Plus provides non-inferior effectiveness and safety compared to PKU Easy Microtabs.

Economic analysis

5.8 The submission presented a cost-minimisation analysis of PKU Easy Microtabs Plus compared to PKU Easy Microtabs, based on the same cost per gram of PE. The proposed approved ex-manufacturer price (AEMP) and dispensed price for maximum quantity (DPMQ) for PKU Easy Microtabs Plus are provided in Table 3.

Table 3: Protein equivalent contents and prices of PKU Easy Microtabs Plus and PKU Easy Microtabs

	PKU Easy Microtabs Plus	PKU Easy Microtabs
AEMP (per pack)	\$252.60 (324 g PE)	\$242.91 (312 g PE)
AEMP (per maximum qty)	\$252.60 x 7 = \$1,768.20 (2,268 g PE)	\$242.91 x 7 = \$1,700.37 (2,181 g PE)
DPMQ	\$1,921.45	\$1,850.21

Source: Table 3-1, pp 27-28 of the main submission

Abbreviation: PE = protein equivalent; AEMP = approved ex-manufacturer price; DPMQ = Dispensed price for maximum quantity

Note: AEMP and DPMQ are as published on the PBS website, accessed on June 2024; each pack of PKU Easy Microtabs Plus and PKU Easy Microtabs contains 6 and 4 tablets respectively.

5.9 The protein equivalent contents and prices of PKU Easy Microtabs Plus and alternative therapies accepted by the Nutritional Products Working Party (NPWP) are provided in the table below.

Table 4: Protein equivalent contents and prices of PKU Easy Microtabs Plus and alternative therapies

Brand Name	PBS item number	PE/ 100 g ^a	Pack size	Max qty packs	PE/Max Qty	AEMP ^c (\$)	DPMQ ^c (\$)
PKU Easy Microtabs Plus	New	54 g	6 x 100	7	2,268 g	252.60	1,921.45
PKU Easy Microtabs	10683G	70.8 g	4 x 110	7	2,181 g	242.91	1,850.21
PKU Easy Tablet	12072J	73 g	6 x 77	4	1,700 g ^b	299.47	1,322.65
Phlexy 10	8678R	83.3 g	1 g x 75	24	1,494 g ^b	43.86	1,170.21

^a Data obtained from the respective sponsors' websites accessed on 19 November 2024

^b Table 1 of PKU Easy Tablet Public Summary Document, November 2019 PBAC Meeting.

^c Based on AEMPs and DPMQs as of June 2024

AEMP = approved ex-manufacturer price, DPMQ = dispensed price for maximum quantity, PE = protein equivalent (g)

5.10 The pre-PBAC response argued that Phlexy 10 and PKU Easy Tablet are not appropriate comparators due to their significantly lower PBS service volumes compared to PKU Easy Microtabs in the 2023 calendar year.

5.11 The estimated drug cost/patient per year would be \$23,057.40, based on 12 scripts per year and DPMQ of \$1,921.45. The actual cost may vary due to variations in individual patient needs.

Estimated PBS usage and financial implications

5.12 The submission used a market share approach to estimate utilisation and financial implications, which are outlined in Table 5.

5.13 The estimated usage of PKU Easy Microtabs Plus was derived from the actual PBS service data for PKU Easy Microtabs from 2020 to 2023, assuming that PKU Easy Microtabs Plus will substitute for PKU Easy Microtabs at 20% in Year 1, increasing to 40% by Year 3, with a script equivalence ratio of 0.96, based on the total amounts of PE contained in each product (0.9 = 2,268 g/2,181 g). The submission assumed that there would be no change to the use of other PBS-listed nutritional products.

5.14 The submission estimated that listing PKU Easy Microtabs Plus would result in a net saving to the PBS/RPBS of \$0 to < \$10 million over six years, ranging from \$0 to < \$10 million in Year 1 to \$0 to < \$10 million in Year 6.

Table 5: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of scripts dispensed	1	1	1	1	1	1
Estimated financial implications of PKU Easy Microtabs Plus						
Cost to PBS/RPBS less co-payment	2	2	2	2	2	2
Estimated financial implications of PKU Easy Microtabs						
Cost to PBS/RPBS less co-payment	3	3	3	3	3	3
Net financial implications						
Net cost to PBS/RPBS	3	3	3	3	3	3

Source: Table 4-5 and Table 4-8 of the submission.

Abbreviations: PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme.

The redacted values correspond to the following ranges:

¹ <500

² \$0 to <\$10 million

³ Net cost saving

5.15 As a Category 3 submission, the economic analysis and financial estimates have not been independently evaluated.

6 NPWP consideration

6.1 The NPWP supported the listing of PKU Easy Microtabs Plus on the PBS under the same conditions as PKU Easy Microtabs for the dietary management of PKU on a cost-minimisation basis to the lowest cost comparator, at an equivalent cost per gram of PE.

6.2 The NPWP advised that PKU Easy Microtabs was an appropriate comparator for PKU Easy Microtabs Plus, and that PKU Easy tablet and Phlexy-10 are also appropriate comparators. The NPWP considered that the currently listed tablet forms of amino

acid formulae are alternative therapeutic options that align with the intended use of PKU Easy Microtabs Plus in patients with PKU.

- 6.3 The NPWP accepted that PKU Easy Microtabs Plus is expected to provide non-inferior clinical benefits and safety compared to PKU Easy Microtabs.
- 6.4 The NPWP noted the sponsor's estimation that listing PKU Easy Microtabs Plus would result in minor savings to the PBS/RPBS.
- 6.5 The NPWP noted that PKU Easy Microtabs Plus does not contain choline and expressed concern about the potential risk of inadequate choline levels during pregnancy if used as the sole source of nutrition. The NPWP suggested the PBAC consider whether an administrative note to this effect is appropriate.

7 PBAC Outcome

- 7.1 The PBAC recommended a General Schedule Restricted Benefit listing of amino acid formula with fat, carbohydrate, vitamins and minerals without phenylalanine tablets (modified release), 54 g protein per 100 g, 100 g, pack of 6 (PKU Easy Microtabs Plus) for the dietary management of phenylketonuria (PKU), under the same circumstances as the current PBS listing for PKU Easy Microtabs.
- 7.2 The PBAC considered that PKU Easy Microtabs Plus should be cost-minimised to the lowest cost comparator accepted by the NPWP (i.e., PKU Easy Microtabs, Phlexy 10, and PKU Easy Tablet) at an equivalent price per gram of protein equivalent.
- 7.3 The PBAC noted and accepted PKU Easy Microtabs as an appropriate comparator and that other phe-free amino acid nutritional products listed for PKU in tablet form; PKU Easy tablet and Phlexy-10, are also reasonable comparators.
- 7.4 The PBAC noted and supported the NPWP advice that PKU Easy Microtabs Plus is expected to provide non-inferior clinical benefits and safety compared to PKU Easy Microtabs.
- 7.5 The PBAC noted that the NPWP expressed concern about the potential risk of inadequate choline levels during pregnancy when PKU Easy Microtabs Plus is used as the sole source of nutrition. However, it considered that a specific caution to this effect in the restriction would not be necessary, as clinical discretion regarding optimal nutrition sources for pregnant women with PKU is preferred, given the specialised care generally provided to these patients.
- 7.6 The PBAC considered the estimated use and estimated minor net saving to the PBS/RPBS over 6 years to be reasonable.
- 7.7 The PBAC advised that PKU Easy Microtabs Plus is suitable for prescribing by nurse practitioners.
- 7.8 The PBAC recommended that the Early Supply Rule should not apply, as it has been the PBAC's view that general nutrients be exempt.

- 7.9 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because PKU Easy Microtabs Plus is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over PKU Easy Microtabs, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met.
- 7.10 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

8 Recommended listing

- 8.1 Add new item:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No.of Rpts	Available brands
AMINO ACID FORMULA WITH FAT, CARBOHYDRATE, VITAMINS AND MINERALS WITHOUT PHENYLALANINE					
amino acid formula with fat, carbohydrate, vitamins and minerals without phenylalanine tablet: modified release, 6 x100 g	NEW	7	7	5	PKU Easy Microtabs Plus
Restriction Summary <input type="checkbox"/> / Treatment of Concept: <input type="checkbox"/>					
Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners					
Restriction type: <input checked="" type="checkbox"/> Restricted benefit					
Indication: Phenylketonuria					

This restriction may be subject to further review. Should there be any changes made to the restriction the Sponsor will be informed.

9 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

10 Sponsor's Comment

The sponsor had no comment.