

5.12 GLYCOMACROPEPTIDE FORMULA WITH LONG CHAIN POLYUNSATURATED FATTY ACIDS AND DOCOSAHEXAENOIC ACID AND LOW IN PHENYLALANINE, Oral liquid, 237 mL, 15 (PKU Sphere Liquid), PKU Sphere Liquid, Vitaflo Australia Pty Limited

1 Purpose of Submission

- 1.1 The Category 3 submission requested a General Schedule Restricted Benefit listing of glycomacropeptide formula with long chain polyunsaturated fatty acids and docosahexaenoic acid and low in phenylalanine, bottle containing oral liquid, 237 mL (PKU Sphere Liquid) for the dietary management of patients with phenylketonuria (PKU).

2 Background

- 2.1 The submission stated that PKU Sphere Liquid 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.

Previous PBAC consideration

- 2.2 PKU Sphere Liquid has not been considered by the Pharmaceutical Benefits Advisory Committee (PBAC) previously.
- 2.3 In March 2022, the PBAC had recommended the General Schedule Restricted Benefit listing of PKU GMP[®] MIX-IN (glycomacropeptide formula with amino acids and low phenylalanine) and PKU GMP[®] ULTRA (glycomacropeptide formula with amino acids, vitamins, minerals, trace elements, carbohydrate, fat and low phenylalanine) for the treatment of PKU.

For more detail on PBAC's view, see section 7 PBAC outcome.

3 Requested listing

- 3.1 The submission requested PKU Sphere Liquid be listed under the same circumstances as PKU Sphere20[®] Powder.
- 3.2 The submission requested the following new listing. Additions are in italics.
Add new medicinal product pack as follows:

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MEDICINAL PRODUCT Medicinal Product Pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
GLYCOMACROPEPTIDE FORMULA WITH LONG CHAIN POLYUNSATURATED FATTY ACIDS AND DOCOSAHEXAENOIC ACID AND LOW IN PHENYLALANINE					
Glycomacropeptide formula with long chain polyunsaturated fatty acids and docosahexaenoic acid and low in phenylalanine oral liquid, 15 x 237 mL bottles	NEW	8	8	5	PKU Sphere Liquid
Restriction Summary [4295] / Treatment of Concept: 4295					
Category / Program: 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					

For more detail on PBAC's view, see section 7 PBAC outcome.

4 Comparator

- 4.1 The submission nominated PKU Sphere20 Powder and PKU GMPro LQ as the main comparators. The submission considered the nutritional profile of PKU Sphere Liquid is similar to the nutritional profile of the comparators (details of the nutritional profile are provided in Table 2). The PBAC considered this was appropriate.

For more detail on PBAC's view, see section 7 PBAC outcome.

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.

Clinical evidence

- 5.3 No clinical trials were presented in the submission comparing PKU Sphere Liquid to the comparators.
- 5.4 The submission cited 3 publications (Table 1) in support of the listing of PKU Sphere Liquid. The submission stated the publications show no differences between Phenylalanine:Tyrosine ratios, anthropometry and nutritional markers between PKU Sphere Powder or a phenylalanine-free amino acid product. PKU Sphere Powder also showed improved palatability over usual amino acid-based formula and improved metabolic control and increased dietary adherence in patients with PKU.

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Table 1: Studies presented in the submission

Author	Publication title	Publication citation
Daly, A	Glycomacropeptide: long-term use and impact on blood phenylalanine, growth and nutritional status in children with PKU	<i>Orphanet J Rare Dis.</i> 2019; 14(1): 44
Daly, A	Growth and body composition in PKU children—A three-year prospective study comparing the effects of L-amino acid to glycomacropeptide protein substitutes	2021; <i>Nutrients.</i> 13(4): 1323
van Calcar SC Johnson EB	Evaluation of acceptability, tolerance, and metabolic control of patients with Phenylketonuria consuming PKU sphere	Poster. Genetic Metabolic Dietitians International; 2022; Las Vegas, USA

Source: Reference list of the submission

- 5.5 The submission claimed the nutrition composition of PKU Sphere Liquid is therapeutically equivalent to PKU Sphere20 Powder and PKU GMPro LQ. The details of the nutritional profile of PKU Sphere Liquid and the comparators are provided in Table 2.
- 5.6 The submission stated one bottle (237 mL) PKU Sphere Liquid provides 497 kJ/ 120 kcal, 20 g protein equivalent (PE); 30 mg phenylalanine, and 109 mg docosahexaenoic acid (DHA).
- 5.7 The submission stated PKU Sphere20 Powder provides 20 g PE per 35 g sachet. PKU GMPro LQ provides 10 g PE per unit (250 mL carton).
- 5.8 The submission stated PKU Sphere Liquid is less concentrated in PE than PKU Sphere20 Powder. The submission considered patients who switch to PKU Sphere Liquid will require more formulation volume per day of PKU Sphere Liquid to maintain the same level of metabolic control as PKU Sphere20 Powder. The submission considered the extra volume of formulation will not introduce additional calories. The submission argued patients are unlikely to feel full and appetite for solid food should remain constant.
- 5.9 The submission stated PKU Sphere Liquid has higher concentration of PE than PKU GMPro LQ and considered patients will require less formulation volume of PKU Sphere Liquid per day to maintain the same level of metabolic control as PKU GMPro LQ. The submission argued PKU Sphere Liquid may improve dietary compliance for patients struggling to consume the large volume. The submission also stated PKU Sphere Liquid contains fewer calories than PKU GMPro LQ. The submission argued this will help patients maintain weight within a healthy weight range.

Table 2: Nutritional composition PKU Sphere Liquid, and main comparators, PKU GMPro LQ and PKU Sphere Powder per 100 mL.

Nutrient per 100mL	PKU Sphere Liquid	PKU GMPro LQ	PKU Sphere Powder*
Energy kJ	207	188	339
kcal	50	45	80
Protein Equivalent g	8.3	4.0	13.3
L-Phenylalanine mg	13	7.2	24
Carbohydrate g	2.8	3.4	4.2
O/W sugars g	1.8	3.0	1.5
Fat g	0.5	1.6	1.1
O/W saturates g	0.0	0.16	0.1

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O/W DHA mg	46	24	73
Vitamins			
Vitamin A RE mcg	110	80	173
Vitamin D3 mcg	2.1	2.5	3.3
Vitamin E mg	1.6	1.3	3.6
Vitamin C mg	9.2	6.2	17
Vitamin K mcg	10	7.0	15
Thiamin mg	0.25	0.2	0.4
Riboflavin mg	0.25	0.2	0.4
Niacin mg	1.4	3.0	6.7
Vitamin B6 mg	0.21	0.1	0.4
Folic Acid mcg	43	20	68
Vitamin B12 mcg	0.7	0.3	1.1
Biotin mcg	5.5	3.1	8.7
Pantothenic Acid mg	0.8	0.5	1.3
Choline mg	84	37.5	133
Minerals			
Sodium mg	110	65	159
Potassium mg	120	82.4	227
Chloride mg	0	44	10
Calcium mg	170	144	266
Phosphorus mg	170	121	226
Magnesium mg	50	26	84
Trace Elements			
Iron mg	3.1	1.4	4.9
Copper mcg	250	100	400
Zinc mg	2.8	0.96	4.9
Manganese mg	0.17	0.1	0.3
Iodine mcg	35	16.2	56
Molybdenum mcg	8.4	5.5	13
Selenium mcg	13	5.5	20
Chromium mcg	5.1	3.3	8
Amino Acids			
L-Alanine	0.35	0.16	0.52
L-Arginine	0.41	0.19	0.63
L-Aspartic Acid	0.55	0.24	0.75
L-Cystine	0.10	0.12	0.01
L-Glutamine	1.14	0.03	1.71
Glycine	0.30	0.54	0.8
L-Histidine	0.30	0.16	0.5
L-Isoleucine	0.60	0.29	0.9
L-Leucine	1.27	0.61	2.0
L-Lysine	0.40	0.17	0.53
L-Methionine	0.12	0.05	0.19
L-Proline	0.68	0.32	1.01
L-Phenylalanine	0.013	0.007	0.024
L-Serine	0.43	0.2	0.64
L-Threonine	0.97	0.45	1.47
L-Tryptophan	0.17	0.10	0.27
L-Tyrosine	0.95	0.35	1.49
L-Valine	0.48	0.35	0.73

Source: Appendix 1 and 2 of the submission,

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*Powdered product is made up to standard dilution as per manufacturer’s recommendation, Standard dilution as per manufacturer recommendations: PKU sphere 1 sachet (35 g) + 120 mL water = Total volume ~150 mL

Clinical claim

5.10 The PBAC considered that the claim of noninferior comparative effectiveness was reasonable.

5.11 The PBAC considered that the claim of noninferior comparative safety was reasonable.

Economic analysis

5.12 The submission presented a cost-minimisation approach of PKU Sphere Liquid compared with PKU Sphere20 Powder, based on the same price per gram PE of \$0.76 at the approved ex-manufacturer price (AEMP).

5.13 The proposed AEMP per maximum quantity PE (\$1,827.68) is the same as the main comparator PKU Sphere20 Powder. The PBAC considered this to be appropriate as PKU Sphere Liquid contains the same PE as PKU Sphere20 Powder.

5.14 The price of PKU Sphere Liquid in comparison to the nominated comparator is presented in the table below.

Table 3: Calculated costs versus comparators

	PKU Sphere Liquid	PKU Sphere20 Powder
Presentation	15 x 237 mL bottle 300 g PE	60 x 20 g sachets 300 g PE
g PE per carton	(15 x 20 g PE = 300 g)	(30 x 20 g PE = 600 g)
AEMP per carton	\$228.46	\$456.92
g PE per maximum quantity	2400 g PE = 8 x 300 g	2400 g PE = 4 x 600 g
AEMP per maximum quantity	\$228.46 x 8 = \$1827.68 (2400 g PE)	\$456.92 x 4 = \$1827.68 (2400 g PE)
AEMP per g PE	\$0.765	\$0.765
DPMQ	\$1983.02	\$1983.02^a

Source: Table 1 of PKU Sphere Liquid submission main document

PE = protein equivalent

^a DPMQ as at 23 June 2022

Drug cost/patient/year: \$23,796.24

5.15 The estimated drug cost/patient per year would be approximately \$23,796.24, based on a proposed DPMQ of \$1,983.02 and the use of 8 cartons (15 x 237 mL bottles per carton) per month.

Estimated PBS utilisation and financial implications

5.16 The submission used a market share approach to predict the utilisation and estimate the financial implications of listing PKU Sphere Liquid.

Table 4: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Number of scripts Sphere Liquid	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹
Cost to PBS/RPBS less copayments ^c	█ ²	█ ²	█ ²	█ ²	█ ²	█ ²
Number of scripts changed listing PKU Sphere20 Powder	-█ ¹	-█ ¹	-█ ¹	-█ ¹	-█ ¹	-█ ¹
Cost to PBS/RPBS less copayments change listing	-█ ²	-█ ²	-█ ²	-█ ²	-█ ²	-█ ²
Net cost to PBS/RPBS	█ ²	█ ²	█ ²	█ ²	█ ²	█ ²

Source: PKU Sphere Liquid UCM Release3 Workbook PBS of the submission

The redacted values correspond to the following ranges:

¹ < 500

² \$0 to < \$10 million

5.17 The submission estimated no financial impact to the PBS/RPBS for the listing of PKU Sphere Liquid as it is expected to substitute within the existing market.

5.18 As a Category 3 submission, neither the economic analysis nor the financial estimates analysis have been independently evaluated.

For more detail on PBAC's view, see section 7 PBAC outcome.

6 NPWP Consideration

6.1 The Nutritional Products Working Party (NPWP) supported the General Schedule Restricted Benefit Listing of PKU Sphere Liquid on a cost-minimisation basis against PKU Sphere20 Powder.

6.2 The NPWP considered the comparators to be appropriate, and also considered PKU Sphere Liquid to be nutritionally very similar to the comparators, well tolerated with good compliance and acceptability, and that the low calorie aspect of PKU Sphere Liquid may assist patients who struggle with weight gain.

6.3 The NPWP considered PKU Sphere Liquid is clinically substitutable at a patient level with PKU Sphere20 Powder, PKU GMPro LQ, PKU Express 20, PKU GMPro MIX-IN and PKU GMPro ULTRA for the treatment of PKU.

For more detail on PBAC's view, see section 7 PBAC outcome.

7 PBAC Outcome

7.1 The PBAC recommended the General Schedule Restricted Benefit listing of glycomacropeptide formula with long chain polyunsaturated fatty acids and docosahexaenoic acid and low in phenylalanine, bottle containing oral liquid, 237 mL (PKU Sphere Liquid) for the dietary management of patients with phenylketonuria under the same circumstances as PKU Sphere20 Powder.

7.2 The PBAC noted and agreed with the NPWP advice detailed in Section 6 NPWP consideration.

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- 7.3 The PBAC advised that PKU Sphere Liquid is suitable for prescribing by nurse practitioners.
- 7.4 The PBAC recommended that the Early Supply Rule should not apply, as it has been the PBAC’s view that general nutrients be exempt.
- 7.5 The PBAC considered the cost-minimisation approach of PKU Sphere Liquid compared with the comparator PKU Sphere20 Powder appropriate, based on the same price per gram protein equivalent of \$0.76.
- 7.6 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because PKU Sphere Liquid is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over PKU Sphere20 Powder, 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.
- 7.7 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 medicinal product pack:

MEDICINAL PRODUCT Medicinal Product Pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
GLYCOMACROPEPTIDE FORMULA WITH LONG CHAIN POLYUNSATURATED FATTY ACIDS AND DOCOSAHEXAENOIC ACID AND LOW IN PHENYLALANINE					
Glycomacropeptide formula with long chain polyunsaturated fatty acids and docosahexaenoic acid and low in phenylalanine oral liquid, 15 x 237 mL bottles	NEW	8	8	5	PKU Sphere Liquid
Restriction Summary [4295] / Treatment of Concept: 4295					
Category / Program: 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.