

**5.27 AMINO ACID FORMULA WITH VITAMINS AND MINERALS WITHOUT LYSINE AND LOW IN TRYPTOPHAN,
Sachets containing oral powder 12.5 g, pack of 30 (GA explore5)
GA explore5™,
VITAFLO AUSTRALIA PTY LIMITED**

1 Purpose of Submission

- 1.1 The Category 3 submission requested a General Schedule Restricted Benefit listing of amino acid formula with vitamins and minerals without lysine and low in tryptophan sachets containing oral powder 12.5 g, 30 (GA explore5™), for the dietary management of patients with proven glutaric aciduria type 1 (GA-1) or pyridoxine dependent epilepsy (PDE).
- 1.2 Listing was requested on the basis of a cost-minimisation approach versus amino acid formula with vitamins and minerals without lysine and low in tryptophan sachets containing oral powder 24 g, 30 (GA gel) at the same cost per gram of protein equivalent (PE).

2 Background

- 2.1 GA explore5 has not been previously considered by the PBAC.
- 2.2 The submission stated that GA explore5 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 listing GA explore5 under the same indications and criteria as the currently listed GA gel (PBS item code: 9438R).

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 VITAMINS AND MINERALS WITHOUT LYSINE AND LOW IN TRYPTOPHAN					
amino acid formula with vitamins and minerals without lysine and low in tryptophan containing 5 g of protein equivalent powder for oral liquid, 30 x 12.5 g sachets	NEW	8	8	5	GA explore5
Restriction Summary 5323/ Treatment of Concept: 5323					
Concept ID (for internal Dept. use)	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				
15792	Indication: Proven glutaric aciduria type 1				
Restriction Summary [11482] / Treatment of Concept: 11482					
Concept ID (for internal Dept. use)	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				
26629	Indication: Pyridoxine dependent epilepsy				
26911	Clinical criteria:				
26910	Patient must be managed on a low lysine diet for pyridoxine dependent epilepsy				
	AND				
10880	Clinical criteria:				
10879	The condition must be treated by or in consultation with a metabolic physician				

- 3.2 The submission requested a maximum quantity of 8 packs/units with 5 repeats for GA explore5 (30 x 12.5 g sachets). This request was based on the current listing for GA gel (30 x 24 g sachets), which has a maximum quantity of 4 packs/units with 5 repeats, providing approximately 1 month of supply, corresponding to 1200 g PE at the maximum quantity. The proposed quantity and repeats for GA explore5 would provide an equivalent amount of PE over the same period.
- 3.3 The submission indicated that if GA explore5 is listed on the PBS, the sponsor intends to delist GA gel.

4 Comparator

- 4.1 The submission nominated GA gel as the main comparator due to its similarity to GA explore5 in nutritional composition and presentation. While GA gel was an appropriate comparator, there are other nutritional products of amino acid formula with vitamins and minerals without lysine and low in tryptophan for the dietary management of GA-1, noting these products are not PBS-listed for PDE (Table 1).

Table 1: PBS-listed nutritional products for the dietary management of GA-1 as of August 2024

Trade name	Form	PBS item code	Max. qty packs	No. of Rpts	AEMP
GA1 Anamix Junior	amino acid formula with vitamins and minerals without lysine and low in tryptophan powder for oral liquid, 30 x 18 g sachets	10715Y	8	5	\$210.33
GA1 Anamix infant	amino acid formula with vitamins and minerals without lysine and low in tryptophan powder for oral liquid, 400 g	2650L	8	5	\$72.92
XLYS, LOW TRY Maxamum	amino acid formula with vitamins and minerals without lysine and low in tryptophan powder for oral liquid, 500 g	10466W	9	5	\$278.62
GA gel	amino acid formula with vitamins and minerals without lysine and low in tryptophan powder for oral liquid, 30 x 24 g sachets	9438R	4	5	\$420.66

PBS = Pharmaceutical Benefits Scheme; AEMP = approved ex-manufacturer price; GA-1 = glutaric aciduria type 1

- 4.2 At the November 2015 PBAC meeting, GA1 Anamix Junior brand of amino acid formula with vitamins and minerals without lysine and low in tryptophan was recommended for listing for GA-1 on a cost-minimisation compared to GA gel at an equivalent price per gram of protein (paragraph 6.1, GA1 Anamix Junior, Public Summary Document (PSD), November 2015 PBAC Meeting).
- 4.3 At its November 2020 meeting, the PBAC recommended the listing of amino acid formula with vitamins and minerals without lysine and low in tryptophan (GA gel and GA express 15 only) for the dietary management of PDE (paragraph 8.1, GA gel, PSD, November 2020 PBAC Meeting). As GA express 15 has been delisted from the PBS since 1 May 2024, GA gel is the only PBS-listed nutritional product indicated for both GA-1 and PDE.

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 The submission noted that GA-1 is an autosomal recessive disorder affecting the metabolism of lysine, hydroxylysine, and tryptophan, with a prevalence of 1 in 100,000 newborns globally¹. Early diagnosis through newborn screening in Australia allows for immediate treatment, preventing neurological damage. PDE is a rare genetic disorder caused by Antiquitin deficiency, leading to intractable seizures

¹ Lindner M., Kolker s., Schulze A., et al., Neonatal screening for glutaryl-CoA dehydrogenase deficiency. *J Inherit Metab Dis.* 2004; 29: 378-382

in newborns and infants due to the accumulation of lysine degradation intermediates. Treatment for both conditions involves dietary management with a restricted protein diet (low lysine/low tryptophan).

Nutritional profile

- 5.4 The submission stated that GA explore5 is nutritionally similar to its main comparator, GA gel. Details of the nutritional profile of GA explore5 and GA gel are provided in Table 2, with key differences between the two products being:
- Long chain polyunsaturated fatty acids (LCPUFAs); arachidonic acid (ARA) and docosahexaenoic acid (DHA), which are essential for brain growth and development, are present in GA explore5 only.
 - GA explore5 is available in a smaller sachet containing 5 g of PE, suitable for older infants and young children, allowing for easy adjustment of dosage to meet their increasing protein needs, while GA gel provides 10 g PE per sachet.
 - GA explore5 contains a newly sourced starch, providing consistency and texture that support the weaning phase and the introduction of solids in older infants and young children.
- 5.5 The submission provided comparisons of the nutritional profile of GA explore5 to Australian Nutrient Reference Values (NRVs) for relevant age groups to demonstrate that GA explore5 contains adequate nutrient content to meet most NRV standards for vitamins, minerals, and trace elements. The submission stated that the levels of DHA and ARA in GA explore5 align with the Australian NRVs and match the ratio found in human breastmilk.
- 5.6 The submission noted that GA explore5 is reconstituted to a semi-solid, spoonable consistency, therefore, osmolality is not applicable due to its product format.
- 5.7 The submission indicated that GA explore5 contains fish (tuna) and is unsuitable for those with a milk allergy.

Table 2: Comparison of nutritional composition: GA explore5 versus GA gel (unflavoured)

Nutrient and unit	per 100 g powder		per 100 kcal	
	GA explore5	GA gel	GA explore5	GA gel
Energy kJ	1450	1440	424	424
kcal	342	339	100	100
Protein Equivalent (PE) g	40	41.7	11.7	12.3
L-Lysine* g	0	0	0	0
L-Tryptophan g	0.31	0.31	0.09	0.09
Carbohydrate g	42	42.9	12.3	12.7
O/W sugars g	28	27.1	8.2	8.0
Fat g	1.5	0.05	0.4	0.01
O/W saturates g	0.7	0.0	0.2	0.0
O/W pufas ^A g	0.5	0	0.15	0
DHA mg	140	0	40	
ARA mg	280	0	80	0
Vitamins				
Vitamin A RE mcg	530	600	155	177
Vitamin D3 mcg	27	14.6	7.9	4.3
Vitamin E mg	9.7	9.0	2.8	2.7
Vitamin C mg	90	63	26	18.6
Vitamin K mcg	27	41	7.9	12.1
Thiamine mg	1.0	1.0	0.3	0.3
Riboflavin mg	1.5	1.2	0.4	0.4
Niacin mg (mg/NE)	6.9 (12)	14 (18.5)	2.0/ (3.5)	4.1/ (9.4)
Vitamin B6 mg	1.1	1.1	0.3	0.3
Folic Acid mcg	230	208	67	61
Vitamin B12 mcg	3.7	2.0	1.1	0.6
Biotin mcg	23	25	6.7	7.4
Pantothenic Acid mg	7.3	5.0	2.1	1.5
Choline mg	450	279	131	82
Minerals				
Sodium mg	195	379	57	119
Potassium mg	500	938	146	277
Chloride mg	500	583	146	172
Calcium mg	1100	1083	321	319
Phosphorus mg	730	825	213	243
Magnesium mg	135	167	39	49
Trace Elements				
Iron mg	16	14	4.7	4.1
Copper mg	0.78	0.8	0.23	0.23
Zinc mg	11	11	3.2	3.2
Manganese mg	0.25	1.7	0.07	0.5
Iodine mcg	150	138	44	41
Molybdenum mcg	40	50	11.7	14.8
Selenium mcg	31	35	9.1	10.3
Chromium mcg	30	71	8.8	21

Source: Appendix 1 and Appendix 1a of the submission

Abbreviations: o/w = oil-in-water; ARA = Arachidonic Acid; DHA: docosahexaenoic acid

Clinical trials

5.8 The submission presented no clinical trials comparing GA explore5 with the main comparator, GA gel, however, it claimed that there is little therapeutic difference between the two products, as noted in paragraph 5.4.

Clinical claim

5.9 The submission claimed that GA explore5 is therapeutically comparable to GA gel.

Economic analysis

5.10 The submission presented a cost-minimisation analysis of GA explore5 compared to GA gel, based on the same cost per gram of PE. The protein equivalent content and proposed price of GA explore5, in comparison to GA gel, are outlined in Table 3.

Table 3: protein equivalent contents and prices of GA explore5 and GA gel

	GA explore5	GA gel
AEMP (per pack)	\$210.33 (150 g PE)	\$420.66 (300 g PE)
AEMP (per maximum qty)	\$210.33 x 8 = \$1,682.64 (1200 g PE)	\$420.66 x 4 = \$1,682.64 (1200 g PE)
DPMQ	\$1,831.65	\$1,831.65*

Source: Table 1 of the main submission

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

Note: AEMP and DPMQ of GA gel are as published on the PBS website, accessed on 5 June 2024; each pack of GA explore5 and GA gel contains 30 sachets.

5.11 The estimated drug cost/patient per year is \$21,979.80 based on 12 scripts per year for the maximum quantity requested at DPMQ of \$1,831.65.

Estimated PBS usage and financial implications

5.12 The submission presented an analysis of the estimated PBS usage and financial implications (see Table 4).

5.13 The submission claimed that the listing of GA explore5 is not expected to result in any new patients commencing dietary therapy for GA-1 and PDE, therefore, GA explore5 would not increase the use of protein substitutes. The submission indicated that prescriptions of GA gel are expected to decline and cease within six to twelve months after GA explore5 is listed, as the sponsor intends to delist GA gel if GA explore5 is recommended.

5.14 The submission estimated that there would be no financial implications of listing GA explore5 to the PBS/RPBS, as GA explore5 will directly substitute for GA gel at the same cost per gram of PE.

Table 4: 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 ^a	¹	¹	¹	¹	¹	¹
Estimated financial implications of GA explore5						
Cost to PBS/RPBS less co-payment (\$)	²	²	²	²	²	²
Estimated financial implications of GA gel						
Cost to PBS/RPBS less co-payment (\$)	- ³	- ³	- ³	- ³	- ³	- ³
Net financial implications						
Net cost to PBS/RPBS (\$)	²	²	²	²	²	²

^a Assuming 12.167 prescriptions per patient per year as estimated by the submission.

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

Source: UCM-Release-3-Workbook

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 GA explore5 as a General Schedule Restricted Benefit for the dietary management of patients with proven GA-1 or PDE on a cost-minimisation basis to the main comparator, GA gel, at an equivalent cost per gram of PE.

6.2 The NPWP noted that GA explore5 is therapeutically comparable to GA gel and considered GA gel as the most appropriate comparator. The NPWP also noted that GA explore5 and GA gel are intended for the dietary management of GA-1 and PDE in infants and children from six months of age, with GA explore5 suitable for ages six months to five years, and GA gel for ages six months to 10 years. In contrast, GA1 Anamix Infant is intended for infants from birth to 12 months, and GA1 Anamix Junior for children aged one to 10 years with GA-1.

6.3 The NPWP accepted that GA explore5 is expected to provide non-inferior clinical benefits and safety compared to GA gel.

6.4 The NPWP supported the sponsor's estimation that the listing of GA explore5 would result in a nil financial impact to the PBS/RPBS.

6.5 The NPWP noted that GA explore5 is not suitable for individuals with a milk allergy but considered that prescribers can manage this. The NPWP also noted that the PDE indication was not included in the datacard provided in the submission. The NPWP asked that the sponsor consider including PDE in the Australian datasheet on its website.

7 PBAC Outcome

- 7.1 The PBAC recommended that amino acid formula with vitamins and minerals without lysine and low in tryptophan sachets containing oral powder 12.5 g, 30 (GA explore5™) be listed on the PBS as a General Schedule Restricted Benefit listing for the dietary management of patients with proven glutaric aciduria type 1 (GA-1) or pyridoxine dependent epilepsy (PDE).
- 7.2 The PBAC noted and accepted the NPWP advice that GA gel is the most appropriate comparator for GA explore5 and recommended that GA explore5 be cost-minimised to GA gel at an equivalent price per gram of protein equivalent.
- 7.3 The PBAC noted and supported the NPWP advice that GA explore5 is expected to provide non-inferior clinical benefits and safety compared to GA gel.
- 7.4 The PBAC considered the estimated use and estimated nil net financial impact to the PBS/RPBS over six years to be reasonable.
- 7.5 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because GA explore5 is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over GA gel, 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.
- 7.6 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 VITAMINS AND MINERALS WITHOUT LYSINE AND LOW IN TRYPTOPHAN					
amino acid formula with vitamins and minerals without lysine and low in tryptophan containing 5 g of protein equivalent powder for oral liquid, 30 x 12.5 g sachets	NEW	8	8	5	GA explore5
Restriction Summary 5323/ Treatment of Concept: 5323					
Concept ID (for internal Dept. use)	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: Proven glutaric aciduria type 1					

Restriction Summary 11482 / Treatment of Concept: 11482	
Concept ID (for internal Dept. use)	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: Pyridoxine dependent epilepsy
	Clinical criteria:
	Patient must be managed on a low lysine diet for pyridoxine dependent epilepsy
	AND
	Clinical criteria:
	The condition must be treated by or in consultation with a metabolic physician

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.