6.05 AMINO ACID FORMULA WITH VITAMINS AND MINERALS WITHOUT LYSINE AND LOW IN TRYPTOPHAN
Oral liquid, 400 g
GA1 Anamix Infant
Powder for oral liquid, 30 x 18 g sachets
GA1 Anamix Junior
Nutricia Australia Pty Ltd

1 Purpose of Submission

1.1 The Committee Secretariat submission requested an extension of the current PBS listings for amino acid formula with vitamins and minerals without lysine and low in tryptophan (Glutaric Aciduria Type 1 (GA1) Anamix Infant and GA1 Anamix Junior) to include use in pyridoxine-dependent epilepsy (PDE) deficiency.

2 Background

Registration status

2.1 GA1 Anamix Infant and GA1 Anamix Junior are marketed as nutritional products and not a therapeutic good, therefore they are not registered in the Australian Register of Therapeutic Goods.

Previous PBAC consideration

2.2 GA1 Anamix Infant (PBS Code: 2650L) and GA1 Anamix Junior (PBS Code: 10715Y) are currently listed on the PBS for the management of GA1.

2.3 GA1 Anamix Infant and GA1 Anamix Junior have not been previously considered by the PBAC for the dietary management of PDE deficiency.

3 Requested listing

3.1 The submission's proposed additions are shown with bold text. Additions and deletions (indicated with strikethrough) proposed by the Secretariat are also shown in italics with regular text.

3.2 Add new restriction summary as follows:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.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 powder for oral liquid, 400 g	2650L MP NP	8	8	5	GA1 Anamix Infant
amino acid formula with vitamins and minerals without lysine and low in tryptophan powder for oral liquid, 30 x 18 g sachets	10715Y MP NP	8	8	5	GA1 Anamix Junior
Restriction Summary / Treatment of Concept					
Concept ID (for internal Dept. use)	**Category / Program:** ☒ GENERAL - General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners ☒Nurse Practitioners				
	Restriction type: ☒Restricted Benefit				
	Indication: Proven glutaric aciduria type 1				
Restriction Summary / Treatment of Concept					
Concept ID *(for internal Dept. use)*	***Category / Program:*** ☒ *GENERAL - General Schedule (Code GE)*				
	Prescriber type: ☒*Medical Practitioners* ☒*Nurse Practitioners*				
	Restriction type: ☒*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				

3.3 The submission proposed no change to the maximum quantity and number of repeats of GA1 products on the PBS when used for PDE deficiency indication. The maximum quantity and number of repeats provide supply for approximately 6 months of therapy.

3.4 The submission did not propose a comparator for the requested extension to include PDE indication. Currently, an amino acid formula with vitamins and minerals, without lysine and low in tryptophan (GA explore5), is listed on the PBS for the management of PDE (PBS Code 14781Y). The associated clinical criteria are: (1) patient must be managed on a low-lysine diet for PDE; and (2) patient must be managed on a low-lysine diet for pyridoxine-dependent epilepsy. The PBAC considered that these clinical criteria should be included in the restriction for consistency.

4 Consideration of the evidence

Sponsor hearing

4.1 There was no hearing for this item.

Consumer inputs

4.2 The PBAC noted that no consumer inputs were received for this item.

Clinical need and place in therapy intervention, availability of alternatives and safety

4.3 The submission described PDE as an ultra-rare metabolic epilepsy caused by ALDH7A1 deficiency, resulting in neurotoxic metabolite accumulation, neonatal-onset seizures, and neurodevelopmental impairment. Standard management included pyridoxine alongside dietary lysine restriction and arginine supplementation to address the underlying metabolic defect.

4.4 The submission proposed no changes to the formulations. The submission described that GA1 Anamix Infant and GA1 Anamix Junior are specialised amino acid–based medical formulas providing lysine-free, low-tryptophan nutrition, contain a balanced blend of essential and non-essential amino acids, carbohydrate, fat, vitamins, minerals, and trace elements, and are intended to meet the nutritional requirements of patients with PDE when used as directed with breast milk or standard infant formula and prescribed arginine supplementation.

4.5 The submission stated GA1 Anamix Infant and GA1 Anamix Junior support dietary lysine restriction, reduce neurotoxic metabolite accumulation and improve long-term neurodevelopmental outcomes in PDE. The submission supported a PBS listing extension based on international guidelines and established clinical practice, acknowledging the limited availability of randomised trial evidence due to the ultra-rare nature of the condition.

Equity and Access Considerations

4.6 The submission considered that, in the absence of PBS subsidisation, families are required to bear the full cost of an essential medical food that forms part of standard-of-care treatment, resulting in inequitable access based on financial capacity. Extending the PBS indication would facilitate subsidised access to a well-established component of PDE management for a small, clearly defined patient population, aligning Australian practice with international standards without introducing new safety concerns or imposing a significant resource burden.

Cost and Estimated PBS usage and financial implications

4.7 The submission proposed no change to the current price of GA1 Anamix Infant and GA1 Anamix Junior for their extension to the dietary management of PDE. A comparison of the prices of GA1 Anamix Infant and GA1 Anamix Junior with the PBS-listed GA Explore 5 for the management of PDE is provided in Table 1.

Table 1: Current prices of GA1 Anamix Infant and GA1 Anamix Junior for the dietary management of GA1 (requested for PDE), and the current price of GA Explore 5 listed for PDE.

	GA explore5	GA1 Anamix Infant	GA1 Anamix Junior
Protein equivalent	150 g	52.4 g	150 g
AEMP (per pack)	$210.33	$72.92	$210.33
DPMQ	$1,831.65	$666.36	$1,831.65

Source: PBS website, AEMP = approved ex-manufacturer price, DPMQ = dispensed price for maximum quantity

4.8 Table 2 presents the estimated extent of use, cost of GA1 Anamix Infant and GA1 Anamix Junior to the PBS/RPBS and the net financial implications to the PBS/RPBS. The financial impact to Services Australia would be determined by that agency as part of the post PBAC process.

4.9 In the provided UCM workbook, the Secretariat noted that the pack size input for GA1 Anamix Junior and GA1 Anamix Infant was entered as 1 for both products. The scripts/treatment values resulted in 360 and 3840, respectively. These inputs resulted in an overestimation of the net financial impact by more than 100-fold.

4.10 The Secretariat amended the pack size inputs for GA1 Anamix Junior and GA1 Anamix Infant to 30 and 400, respectively, which revised the scripts/treatment values to 12 and 9.6. Table 2 below presents the resulting net impact. On this basis, the Secretariat considers that the estimated net financial impact to the PBS/RPBS for listing GA1 Anamix Infant and GA1 Anamix Junior should be $0 to < $10 million over six years, rather than $70 million to < $80 million (Year 1: $0 to < $10 million instead of $0 to < $10 million; Year 6: $0 to < $10 million instead of $10 million to < $20 million).

Table 2: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Total all patients	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Estimated extent of use						
Number of scripts dispensed GA1 Anamix Junior	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Number of scripts dispensed GA1 Anamix infant	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Estimated total volume of medicine	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Sponsor's estimated aggregate financial implications of GA1 Anamix Junior and GA1 Anamix Infant						
New listing Cost to PBS/RPBS less co-payment	$[redacted][2]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]
Changed listing Cost to PBS/RPBS less co-payment	$0	$0	$0	$0	$0	$0
Net financial implications – sponsor's estimation (this is overestimated)						
Net cost to PBS/RPBS	$[redacted][2]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]	$[redacted][3]
PBAC Secretariat' amendment to the financial implications of GA1 Anamix Junior and GA1 Anamix Infant						
Net cost to PBS/RPBS	$[redacted][2]	$[redacted][2]	$[redacted][2]	$[redacted][2]	$[redacted][2]	$[redacted][2]

Abbreviations: PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme.
Source: Submission UCM workbook.
The redacted values correspond to the following ranges:
[1] *< 500*
[2] *$0 to < $10 million*
[3] *$10 million to < $20 million*

4.11 As a Committee Secretariat submission, the economic analysis and financial estimates have not been independently evaluated.

5 NPWP consideration

5.1 The NPWP advised that it supports extending the current PBS listings for GA1 Anamix Infant and GA1 Anamix Junior to include dietary management of pyridoxine-dependent epilepsy deficiency (PDE) deficiency.

5.2 The NPWP advised that GA1 Anamix Infant and GA1 Anamix Junior meet the dietary requirements for the management of PDE and, in the absence of suitable alternatives in Australia, may represent the standard of care for this condition.

5.3 The NPWP considered that only a small patient population in Australia is likely to require dietary management of PDE deficiency.

5.4 The NPWP advised that the current maximum quantity of eight packs and five repeats is appropriate for the dietary management of PDE.

5.5 The NPWP advised that the existing PBS safety profile of GA1 products can reasonably be extrapolated to PDE deficiency, with no need for additional risk-management measures.

6 PBAC Outcome

6.1 The PBAC recommended extending the current General Schedule Restricted Benefit listings for amino acid formula with vitamins and minerals without lysine and low in tryptophan (Glutaric Aciduria Type 1 (GA1) Anamix Infant and GA1 Anamix Junior) to include use in pyridoxine-dependent epilepsy (PDE) deficiency.

6.2 The PBAC noted that the NPWP had supported extending the use of PBS-listed GA1 products to include the dietary management of PDE deficiency.

6.3 The PBAC recommended that the associated clinical criteria for the currently listed amino acid formula with vitamins and minerals without lysine and low in tryptophan (GA explore5) be included in the restrictions for GA1 Anamix Infant and GA1 Anamix Junior for the management of PDE for consistency. The PBAC also considered that the proposed maximum quantity of eight packs and five repeats, permitting prescribing by both medical practitioners and nurse practitioners to be appropriate for the management of PDE. The PBAC recommended no change to the current prices of GA1 Anamix Infant and GA1 Anamix Junior for the proposed extension to include dietary management of PDE deficiency.

6.4 The PBAC noted the NPWP advice that only a small patient population in Australia is likely to require dietary management of PDE deficiency. The PBAC considered the Secretariat's estimate of the financial implications to be appropriate.

6.5 The PBAC found that the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met, as its recommendation to amend the current PBS listing GA1) Anamix Infant and GA1 Anamix Junior to include patients diagnosed with PDE deficiency is not expected to address a high and urgent unmet clinical need.

6.6 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:
Recommended

7 Recommended listing

7.1 Add new restriction summary to **GA1 Anamix Infant and GA1 Anamix Junior** as follows:

MEDICINAL PRODUCT **medicinal product pack**	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.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 powder for oral liquid, 400 g	2650L MP NP	8	8	5	GA1 Anamix Infant
amino acid formula with vitamins and minerals without lysine and low in tryptophan powder for oral liquid, 30 x 18 g sachets	10715Y MP NP	8	8	5	GA1 Anamix Junior
Restriction Summary / Treatment of Concept					
Concept ID (for internal Dept. use)	**Category / Program:** ☒ GENERAL - General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners ☒Nurse Practitioners				
	Restriction type: ☒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.

8 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.

9 Sponsor's Comment

The sponsor had no comment.