

**5.28 AMINO ACID FORMULA WITH VITAMINS AND MINERALS WITHOUT METHIONINE, THREONINE AND VALINE AND LOW IN ISOLEUCINE, Sachets containing oral powder 12.5 g, pack of 30 (MMA/PA explore5), MMA/PA 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 methionine, threonine and valine and low in isoleucine, sachets containing oral powder 12.5 g, 30 (MMA/PA explore5™) for the dietary management of patients with a proven diagnosis of methylmalonic acidaemia (MMA) or propionic acidaemia (PA).
- 1.2 Listing was requested on a cost-minimisation basis versus amino acid formula with vitamins and minerals without methionine, threonine and valine and low in isoleucine, sachets containing oral powder 18 g, 30 (MMA/PA Anamix Junior) at the same cost per gram of protein equivalent (PE).

**2 Background**

- 2.1 MMA/PA explore5 has not been previously considered by the PBAC.
- 2.2 The submission stated that MMA/PA 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 the listing of MMA/PA explore5 under the same conditions as the current listings for MMA/PA Anamix Junior and MMA/PA Anamix Infant (PBS item codes: 10730R, 8058D).

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 METHIONINE, THREONINE AND VALINE AND LOW IN ISOLEUCINE					
amino acid formula with vitamins and minerals without methionine, threonine and valine and low in isoleucine containing 5 g of protein equivalent powder for oral liquid, 30 X 12.5 g sachets	NEW	8	8	5	MMA/PA explore5
<b>Restriction Summary 6055/ Treatment of Concept: 6055</b> [as per PBS item code: 10730R]					
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: Methylmalonic acidaemia					
<b>Restriction Summary 5986/ Treatment of Concept: 5986</b> [as per PBS item code: 10730R]					
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: Propionic acidaemia					

- 3.2 The submission requested that MMA/PA explore5 be listed with the same maximum quantity of 8 and 5 repeats as MMA/PA Anamix Junior, which provides a month's supply of 1200 g PE per prescription when dispensed at the maximum quantity.

## 4 Comparator

- 4.1 The submission nominated the currently PBS-listed MMA/PA Anamix Junior and MMA/PA Anamix Infant for the dietary management of MMA and PA as the main comparators due to their similarity in nutritional composition and presentation to MMA/PA explore5.
- 4.2 There is another nutritional product of amino acid formulation with vitamins and minerals without methionine, threonine and valine and low in isoleucine, sachets containing oral powder 25 g, 30 (MMA/PA express 15) listed for MMA and PA.
- 4.3 MMA/PA express 15 (previously listed as MMA/PA express) and MMA/PA gel were recommended by the PBAC for listing at the same cost per gram of protein as XMTVI Maxamaid (March 2010 PBAC Outcomes), and MMA/PA Anamix Junior was recommended by the PBAC on a cost-minimisation basis against MMA/PA gel and XMTVI Maxamaid at an equivalent price per gram of protein (paragraph 6.1, MMA/PA Anamix Junior, 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 MMA and PA are extremely rare disorders of propionate metabolism. These conditions share biochemical and clinical features due to the accumulation of propionyl-CoA and other toxic metabolites, causing symptoms from severe neonatal acidosis to developmental delays. Treatment aims to reduce toxic metabolite production through dietary protein restriction. Dietary management of MMA and PA focuses on balancing protein intake for growth while avoiding excessive amounts that could trigger metabolic instability in infants and young children.

### ***Nutritional profile***

5.4 The submission stated that the nutritional composition of MMA/PA explore5 is similar to that of the main comparators MMA/PA Anamix Junior and MMA/PA Anamix Infant. Comparisons of the nutritional profile of MMA/PA Explore5, MMA/PA Anamix Junior and MMA/PA Anamix Infant are provided in Table 1. The submission noted that key differences between these products include:

- Intended age: MMA/PA explore5 is suitable for infants and children aged six months to five years, while MMA/PA Anamix Infant is for those from birth to one year, and MMA/PA Anamix Junior is intended for use after one year of age.
- Fatty acid profile: MMA/PA explore5 and MMA/PA Anamix Infant contain the long chain polyunsaturated fatty acids (LCPUFAs): arachidonic acid (ARA) and docosahexaenoic acid (DHA), whereas MMA/PA Anamix Junior does not contain ARA.
- Consistency of formulation: MMA/PA explore5 is designed to provide a low volume and a semi-solid consistency that supports weaning and the introduction of solid foods. This formula provides a concentrated protein source, which may increase compliance as protein requirements rise. MMA/PA Anamix Junior and MMA/PA Anamix Infant are intended to be taken as liquids.

5.5 The submission stated that MMA/PA explore5 is reconstituted as a semi-solid, therefore, osmolality is not applicable due to its product format.

5.6 MMA/PA explore5 contains fish (tuna) and is unsuitable for those with a milk allergy.

Table 1: Nutritional composition: MMA/PA explore5, MMA/PA Anamix Junior and MMA/PA Anamix Infant

Nutrient and unit	MMA/PA explore5 (Unflavoured)	MMA/PA Anamix Infant	MMA/PA Anamix Junior	MMA/PA explore5 (Unflavoured)	MMA/PA Anamix Infant	MMA/PA Anamix Junior
	per 100 g powder			per 100 kcal		
<b>Energy kJ</b>	1450	1950	1538	424	410	415
<b>kcal</b>	342	466	367	100	100	100
<b>Protein Equivalent (PE) g</b>	40	13.1	28	11.7	2.8	7.7
<b>Amino Acid</b>						
L-Methionine g	Nil	Nil	Nil	Nil	Nil	Nil
L-Threonine g	Nil	Nil	Nil	Nil	Nil	Nil
L-Valine g	Nil	Nil	Nil	Nil	Nil	Nil
L-Isoleucine g	0.13	<0.045	<0.025	0.04	<0.009	<0.007
L-Alanine	4.12	1.6	3.42	NP		
L-Arginine	4.23	1.4	3.0			
L-Aspartic Acid	7.35	1.27	2.72			
L-Cystine	1.79	0.51	1.56			
L-Glutamine	5.01	0.13	3.61			
Glycine	1.96	0.64	1.37			
L-Histidine	2.79	0.94	2.02			
L-Leucine	5.81	2.12	4.54			
L-Lysine	4.52	1.43	3.05			
L-Phenylalanine	2.79	0.93	1.99			
L-Proline	2.04	0.64	1.37			
L-Serine	3.05	0.89	1.98			
L-Tryptophan	1.15	0.41	0.69			
L-Tyrosine	2.79	0.93	1.99			
L-Carnitine (mg/100 g)	44	10.1	20			
Taurine (mg/100 g)	88	30	60			
<b>Carbohydrate g</b>	42	50.1	30	12.3	10.5	8.1
<b>O/W sugars g</b>	28	7.5	3.1	8.2	1.6	0.8
<b>Fat g</b>	1.5	23	12.5	0.4	4.8	3.4
<b>O/W saturates g</b>	0.7	7.7	2	0.2	1.6	0.5
DHA mg	140	120	180	40	25	49
ARA mg	280	120	Nil	80	25	Nil
<b>Vitamins</b>						
Vitamin A RE mcg	530	408	525	155	86	142
Vitamin D3 mcg	27	11.2	26.3	7.9	2.4	7.1
Vitamin E mg	9.7	9.23	10.5	2.8	1.9	2.8
Vitamin C mg	90	48.9	52.5	26	10.3	14.2
Vitamin K mcg	27	37.3	17.5	7.9	7.8	4.7
Thiamine mg	1.0	0.51	0.91	0.3	0.1	0.2
Riboflavin mg	1.5	0.51	0.91	0.4	0.1	0.2
Niacin mg (mg/NE)	6.9 (26)	2.33/ (9.16)	2.5/ (14)	2.0/ (7.5)	0.5/ 1.9	0.7/ (3.8)
Vitamin B6 mg	1.1	0.51	0.91	0.3	0.1	0.2
Folic Acid mcg	230	55	263	67	11.6	71
Vitamin B12 mcg	3.7	1.21	1.6	1.1	0.3	0.4
Biotin mcg	23	18.2	14	6.7	3.8	3.8
Pantothenic Acid mg	7.3	2.81	5.3	2.1	0.6	1.4
Choline mg	450	146	280	131	31	76

<b>Minerals</b>						
Sodium mg	195	191	385	57	40	104
Potassium mg	500	505	613	146	106	166
Chloride mg	500	355	560	146	75	151
Calcium mg	1100	410	1348	321	86	364
Phosphorus mg	730	300	885	213	63	239
Magnesium mg	135	58.3	154	39	12	42
<b>Trace Elements</b>						
Iron mg	16	7.92	13.6	4.7	1.7	3.7
Copper mg	0.78	0.42	0.78	0.23	0.09	0.21
Zinc mg	11	5.59	6.6	3.2	1.2	1.8
Manganese mg	0.25	0.029	1.3	0.07	0.006	0.35
Iodine mcg	150	98	174	44	21	47
Molybdenum mcg	40	12.1	35	11.7	2.5	9.5
Selenium mcg	31	17.7	38.5	9.1	3.7	10.4
Chromium mcg	30	14.0	14	8.8	2.9	3.8

Source: Appendices 1 to 2 of the submission;

Abbreviations: o/w = oil-in-water; ARA = Arachidonic Acid ,DHA = Docosahexaenoic Acid , NP = not provided

### **Clinical trials**

5.7 The submission presented no clinical trials comparing MMA/PA explore5 with the main comparators, MMA/PA Anamix Junior and MMA/PA Anamix Infant.

### **Clinical claim**

5.8 The submission claimed that MMA/PA explore5 is therapeutically comparable to MMA/PA Anamix Junior and MMA/PA Anamix Infant.

### **Economic analysis**

5.9 The submission presented a cost-minimisation analysis of MMA/PA explore5 compared to MMA/PA Anamix Junior, based on the same cost per gram of PE. While MMA/PA Anamix Infant is also a main comparator, it was excluded from the economic analysis as the submission claimed MMA/PA Anamix Infant is an infant protein substitute whereas MMA/PA explore5 and MMA/PA Anamix Junior are ‘second-stage’ protein substitutes.

5.10 The protein equivalent content and proposed price of MMA/PA explore5, in comparison to MMA/PA Anamix Junior, are outlined in Table 2.

**Table 2: protein equivalent contents and prices of MMA/PA explore5, MMA/PA Anamix Junior and MMA/PA Anamix Infant**

	<b>MMA/PA Explore5</b>	<b>MMA/PA Anamix Junior</b>	<b>MMA/PA Anamix Infant</b>
<b>AEMP (per pack)</b>	\$199.81 (150 g PE)	\$199.81 (150 g PE)	\$69.27 (52.4 g PE)
<b>AEMP (per maximum qty)</b>	\$199.81 x 8 = \$1,598.48 (1200 g PE))	\$199.81 x 8 = \$1,598.48 (1200g PE)	\$69.27 x 8 = \$554.16 (419.2g PE)
<b>DPMQ</b>	\$1,743.25	\$1,743.25	\$633.65

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 MMA/PA Anamix Junior and MMA/PA Anamix Infant are as published on the PBS website, accessed on 5 June 2024

5.11 The submission estimated that the drug cost/patient per year to be \$21,210.12, assuming that a patient uses the maximum quantity of 8 units per prescription and 12.167 prescriptions per year.

**Estimated PBS usage and financial implications**

5.12 The submission presented an analysis of the estimated PBS usage and financial implications as shown in

5.13 Table 3.

5.14 The submission assumed that MMA/PA explore5 will substitute for MMA/PA Anamix Junior and MMA/PA Anamix Infant without impacting the overall market size. As the proposed listing was at the same cost per gram of PE as MMA/PA Anamix Junior, the submission estimated that the listing of MMA/PA explore5 would be cost-neutral to the PBS/RPBS.

5.15 To estimate the financial impact of listing MMA/PA explore5, the submission used a market share approach based on PBS service data for MMA/PA gel, which was delisted from the PBS on 1 May 2024, rather than using data from currently PBS-listed comparators, MMA/PA Anamix Junior and MMA/PA Anamix Infant. The submission stated that this approach was chosen to enable more realistic forecasting, given that patient numbers are expected to be extremely low (less than one patient).

**Table 3: Estimated use and financial implications**

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
<b>Estimated extent of use</b>						
Number of scripts dispensed <sup>a</sup>	1	1	1	1	1	1
<b>Estimated financial implications of MMA/PA explore5</b>						
Cost to PBS/RPBS less co-payment	2	2	2	2	2	2
<b>Estimated financial implications of MMA/PA gel</b>						
Cost to PBS/RPBS less co-payment	3	3	3	3	3	3
<b>Net financial implications</b>						
Net cost to PBS/RPBS	2	2	2	2	2	2

<sup>a</sup> 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

5.16 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 MMA/PA explore5 as a General Schedule Restricted Benefit for the dietary management of patients with a proven diagnosis of MMA or PA on a cost-minimisation basis to the lowest cost comparator, at an equivalent cost per gram of PE.

- 6.2 The NPWP advised that the nominated comparators, MMA/PA Anamix Junior and MMA/PA Anamix Infant, were appropriate. The NPWP noted that MMA/PA explore5 is intended for use in infants and children aged six months to five years, while MMA/PA Anamix Infant is intended for infants from birth to 12 months, and MMA/PA Anamix Junior is for children aged one to 10 years. MMA/PA express 15 is not considered an alternative therapy for MMA/PA explore5.
- 6.3 The NPWP accepted that MMA/PA explore5 is expected to provide non-inferior clinical benefits and safety compared to MMA/PA Anamix Junior and MMA/PA Anamix Infant.
- 6.4 The NPWP agreed with the sponsor's estimation that listing MMA/PA explore5 would have no financial implications to the PBS/RPBS.

## **7 PBAC Outcome**

- 7.1 The PBAC recommended a General Schedule Restricted Benefit listing of amino acid formula with vitamins and minerals without methionine, threonine and valine and low in isoleucine, sachets containing oral powder 12.5 g, 30 (MMA/PA explore5™) for the dietary management of patients with a proven diagnosis of methylmalonic acidaemia (MMA) or propionic acidaemia (PA), under the same circumstances as the current listings for MMA/PA Anamix Junior and MMA/PA Anamix Infant.
- 7.2 The PBAC considered that MMA/PA explore5 should be cost-minimised to the lowest cost comparator accepted by the NPWP (i.e., MMA/PA Anamix Junior and MMA/PA Anamix Infant) at an equivalent price per gram of protein equivalent.
- 7.3 The PBAC accepted the NPWP advice that the nominated comparators, MMA/PA Anamix Junior and MMA/PA Anamix Infant, were appropriate, noting the different intended age groups for these nutritional products, while MMA/PA express 15 was not considered an alternative therapy for MMA/PA explore5.
- 7.4 The PBAC noted and supported the NPWP advice that MMA/PA explore5 is expected to provide non-inferior clinical benefits and safety for the listed indications compared to MMA/PA Anamix Junior and MMA/PA Anamix Infant.
- 7.5 The PBAC considered the estimated use and estimated nil net financial impact to the PBS/RPBS over 6 years to be reasonable.
- 7.6 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because MMA/PA explore5 is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over MMA/PA Anamix Junior and MMA/PA Anamix Infant, 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 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 METHIONINE, THREONINE AND VALINE AND LOW IN ISOLEUCINE					
amino acid formula with vitamins and minerals without methionine, threonine and valine and low in isoleucine containing 5 g of protein equivalent powder for oral liquid, 30 X 12.5 g sachets	NEW	8	8	5	MMA/PA explore5
<b>Restriction Summary 6055/ Treatment of Concept: 6055</b> [as per PBS item code: 10730R]					
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: Methylmalonic acidaemia					
<b>Restriction Summary 5986/ Treatment of Concept: 5986</b> [as per PBS item code: 10730R]					
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: Propionic acidaemia					

***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.