

5.15 AMINO ACID FORMULA WITH VITAMINS AND MINERALS, WITHOUT PHENYLALANINE AND TYROSINE AND SUPPLEMENTED WITH ARACHIDONIC ACID AND DOCOSAHEXAENOIC ACID

Sachets containing oral powder 12.5 g, 30 (TYR explore5),

TYR 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 phenylalanine and tyrosine and supplemented with arachidonic acid and docosahexaenoic acid (TYR explore5), for the dietary management of tyrosinaemia (TYR).

2 Background

- 2.1 The submission stated that TYR explore5 is a phenylalanine and tyrosine free, protein substitute that contains essential and non-essential amino acids, carbohydrate, vitamins, minerals, trace elements and two long chain polyunsaturated fatty acids (LCPUFAs), arachidonic acid (ARA) and docosahexaenoic acid (DHA).
- 2.2 It is expected that TYR explore5 will largely be used to treat infants and young children from 6 months to 5 years of age.
- 2.3 Amino acid formula with vitamins and minerals without phenylalanine and tyrosine (TYR gel) is currently listed on the PBS as a General Schedule Restricted Benefit for TYR.

Registration status

- 2.4 The submission stated that TYR explore5 complies with the standard for foods for medical purposes as set out under *The Australia New Zealand Food Standards Code – Standard 2.9.5: Food for Special Medical Purposes*.
- 2.5 As TYR explore5 is marketed as a nutritional product and not a therapeutic good, it is not registered in the Australian Register of Therapeutic Goods.

Previous PBAC consideration

- 2.6 TYR explore5 has not been considered by the PBAC for TYR previously.

3 Requested listing

3.1 The submission requested TYR explore5 be listed under the same circumstances as TYR gel. The requested maximum quantity for TYR explore5 was 8 cartons, compared to the current PBS listing of TYR gel which has a maximum quantity of 4 cartons. The maximum quantity of 8 cartons provides the same quantity of protein equivalent (PE) as the current TYR gel listing.

3.2 The submission requested the following new listing. Suggested additions are in italics.

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
<i>AMINO ACID FORMULA WITH VITAMINS AND MINERALS, WITHOUT PHENYLALANINE, TYROSINE AND SUPPLEMENTED WITH ARACHIDONIC ACID AND DOCOSAHEXAENOIC ACID</i>					
<i>amino acid formula with vitamins and minerals, without phenylalanine, tyrosine and supplemented with arachidonic acid and docosahexaenoic acid containing 5 g of protein equivalent powder for oral liquid, 30 x 12.5 g sachets</i>	<i>NEW</i>	<i>8</i>	<i>8</i>	<i>5</i>	<i>TYR explore5</i>
Restriction Summary / Treatment of Concept:					
	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: Tyrosinaemia				

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

4 Comparator

4.1 The submission nominated TYR gel and TYR cooler 10 as comparators. The PBAC considered this to be an appropriate comparator and considered that the alternative comparators identified by the NPWP for the treatment of TYR would be appropriate alternate therapies.

The Nutritional Products Working Party (NPWP) identified the following alternative comparators:

- TYR Anamix infant
- TYR Anamix Junior

4.2 The PBAC noted TYR gel was previously recommended on the basis of cost minimisation to Xphen, Tyr Maxamaid, and there are other comparators which have been cost-minimised to Xphen, Tyr Maxamaid which have not been included as comparators, but these were not identified as alternate comparators by the NPWP.

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 trials

5.3 The submission did not provide any clinical trials that included TYR explore5.

5.4 The submission provided clinical trial data of “A 4 week study evaluating the acceptability of PKU explore5 a new phenylalanine free protein substitute for children” to support its argument that PKU explore5 and TYR explore5 are very similar in formulation and thus TYR explore5 should have the same palatability of PKU explore5. The PBAC noted PKU explore appears to have significant formulation differences compared with TYR explore5 and is used for a different indication.

5.5 As a Category 3 submission, no evaluation of the clinical evidence was undertaken.

Clinical claim

5.6 The submission claimed non-inferior comparative effectiveness and non-inferior comparative safety of TYR explore5 compared with TYR gel. The submission provided a comparison of the nutritional profile of TYR explore5 with TYR gel presented as Table 1.

5.7 The PBAC advised TYR explore5 is expected to provide a non-inferior clinical benefit for the management of TYR compared to the comparators identified.

5.8 The submission also made claims throughout the main body relating to potential additional benefits of TYR explore5 over the comparator. As the submission presented a cost-minimisation analysis with claim of therapeutic equivalence/ non-inferiority, the PBAC did not provide advice on the claimed potential benefits.

Table 1: Nutritional composition of TYR explore5 and nominated comparator TYR gel

Nutrient per 100g powder	TYR explore5 (Unflavoured)	TYR gel (Unflavoured)
Energy kJ	1450	1440
kcal	342	339
Protein Equivalent g	40	41.7
L-Phenylalanine* mg	-	0
L-Tyrosine* mg	-	0
Carbohydrate g	42	42.9

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O/W sugars g	28	27.1
Fat g	1.5	0.05
O/W saturates g	0.7	0.0
O/W pufas ^A g	0.5	<0.05
DHA mg	140	-
Vitamins		
Vitamin A RE mcg	530	600
Vitamin D3 mcg	27	14.6
Vitamin E mg	9.7	9.0
Vitamin C mg	90	63
Vitamin K mcg	27	41
Thiamine mg	1.0	1.0
Riboflavin mg	1.5	1.2
Niacin mg (mg/NE)	6.9 (25)	14 (32.5)
Vitamin B6 mg	1.1	1.1
Folic Acid mcg	230	208
Vitamin B12 mcg	3.7	2.0
Biotin mcg	23	25
Pantothenic Acid mg	7.3	5.0
Choline mg	450	279
Minerals		
Sodium mg	195	379
Potassium mg	500	938
Chloride mg	500	583
Calcium mg	1100	1083
Phosphorus mg	730	825
Magnesium mg	135	167
Trace Elements		
Iron mg	16	14
Copper mg	0.78	0.8
Zinc mg	11	11
Manganese mg	0.25	1.7
Iodine mcg	150	138
Molybdenum mcg	40	50
Selenium mcg	31	35
Chromium mcg	30	71
Amino Acid (g/ 100g powder)		
L-Alanine	3.01	3.12
L-Arginine	3.70	3.83
L-Aspartic Acid	5.71	5.92
L-Cystine	1.38	1.43
L-Glutamine	3.50	3.79
Glycine	3.01	3.12
L-Histidine	2.02	2.09
L-Isoleucine	3.35	3.48
L-Leucine	5.37	5.57
L-Lysine	3.82	3.97
L-Methionine	0.86	0.89
L-Proline	3.10	3.21
L-Serine	2.36	2.45
L-Threonine	2.58	2.67

L-Tryptophan	1.08	1.11
L-Valine	3.65	3.79
L-Carnitine (mg/100g)	44	46
Taurine (mg/100g)	88	92

Source: Appendix 1 and 2 of the submission

*No added Phenylalanine or Tyrosine. These may be present in trace amounts from other ingredients (<10 mg/100 g powder, <4 mg/serving).

^ pufas – polyunsaturated fatty acids

Economic analysis

5.9 The submission presented a cost-minimisation analysis of TYR explore5 compared with TYR gel, based on the same price per gram of PE of \$1.33 at the approved ex-manufacturer price (AEMP) (Table 2).

Table 2: Calculated costs versus comparators

	TYR explore5	TYR gel	TYR Cooler 10
Presentation	30 x 12.5 g sachets 150 g PE	30 x 24 g sachets 300 g PE	30 x 87 mL pouches 300 g PE
g PE per carton	(30 x 5 g PE = 150 g)	(30 x 10 g PE = 300 g)	(30 x 10 g PE = 300 g)
AEMP per carton	\$199.815	\$399.63	\$399.63
g PE per maximum quantity	1200 g PE = 8 x 150 g	1200 g PE = 4 x 300 g	1200 g PE = 4 x 300 g
AEMP per maximum quantity	\$199.815 x 8 = \$1598.52* (1200 g PE)	\$399.63 x 4 = \$1598.52 (1200 g PE)	\$399.63 x 4 = \$1598.52 (1200 g PE)
AEMP per g PE	\$1.33	\$1.33	\$1.33
DPMQ	\$1742.46	\$1742.46 ^a	\$1742.46 ^a

Source: Submission main body, Table 1 p.15

PE = Protein equivalent

^aDPMQ as at December 2022

* Submission table had this number as \$1599.52, which, based on the preceding calculation is understood to be a typographical error. This has been updated here to \$1598.52.

Drug cost/patient/year: \$21,200.51

5.10 The estimated drug cost/patient per year would be \$21,200.51 based on the proposed Dispensed Price for Maximum Quantity (DPMQ) of \$1742.46 and the use of 8 cartons per 12.167 prescriptions per year.

Estimated PBS usage and financial implications

5.11 The submission used a market share approach to predict the utilisation and estimate the financial implications of TYR explore5 against the comparator.

5.12 Table 3 presents the estimated extent of use, cost of TYR explore5 to the PBS/RPBS and the net financial implications to the PBS/RPBS that was included in the submission.

5.13 The submission estimated no net financial impact to the PBS/RPBS for the listing of TYR explore5 over six years (Year 1 \$0 to Year 6 \$0) as the product is expected to substitute within the existing market and not impact overall utilisation.

- 5.14 The PBAC supported the sponsor’s estimation that the new listing would not be expected to result in a change in overall utilisation or financial impact to Government.
- 5.15 The submission stated that TYR explore5 has been developed to replace TYR gel. If TYR explore5 was recommended for PBS listing the sponsor indicated it would request the delisting of TYR gel from the PBS.

Table 3: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of patients treated	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹
Number of scripts dispensed ^a	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹
Estimated financial implications of TYR explore5						
Cost to PBS/RPBS less co-payment (\$)	█ ²	█ ²	█ ²	█ ²	█ ²	█ ²
Estimated financial implications of TYR gel						
Cost to PBS/RPBS less co-payment (\$)	█ ³	█ ³	█ ³	█ ³	█ ³	█ ³
Net financial implications						
Net cost to PBS/RPBS	\$0	\$0	\$0	\$0	\$0	\$0

Source: Vitaflo TYR explore5 UCM Workbook November22

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

^a Assuming 12.167¹ per patient per year as estimated by the submission.

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, 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 NPWP supported the listing of TYR explore5 as a General Schedule Restricted Benefit for the dietary management of TYR on a cost-minimisation basis to the lowest cost comparator on a price per gram of PE basis.
- 6.2 The NPWP advised that TYR gel was an appropriate comparator for TYR explore5, and TYR Anamix infant and TYR Anamix Junior are also alternate comparators.
- 6.3 The NPWP advised that TYR explore5 is nutritionally similar to the comparators and would provide a non-inferior clinical benefit in the management of TYR.
- 6.4 The NPWP advised that TYR explore5 is interchangeable with the comparators at the prescribing level.
- 6.5 The NPWP agreed with the sponsor’s estimation that listing TYR explore5 on the PBS would result in a nil financial impact to the PBS/RPBS.

- 6.6 The NPWP noted that it would be beneficial for patients and clinicians for the sponsor to provide communications on any intent to delist the TYR gel product as soon as possible to allow time for patients to be transitioned onto alternative products.

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 amino acid formula with vitamins and minerals, without phenylalanine and tyrosine and supplemented with arachidonic acid and docosahexaenoic acid (TYR explore5), for the dietary management of tyrosinaemia (TYR) under the same circumstances as TYR gel, except with a maximum quantity of 8 cartons rather than 4 cartons to provide the same number of grams of PE.
- 7.2 The PBAC considered that TYR explore5 should be cost-minimised to the lowest cost comparator accepted by the NPWP (TYR gel, TYR Anamix infant or TYR Anamix Junior), at an equivalent price per gram of PE.
- 7.3 The PBAC noted and supported the NPWP advice that TYR explore5 is nutritionally similar to the comparators and would provide a non-inferior clinical benefit in the management of TYR.
- 7.4 The PBAC considered the estimated use and estimated nil net financial impact to the PBS/RPBS over 6 years to be reasonable.
- 7.5 The NPWP advised that TYR explore5 is interchangeable with the comparators (TYR gel, TYR Anamix infant and TYR Anamix Junior) at the prescribing level.
- 7.6 The PBAC advised that TYR explore5 is suitable for prescribing by nurse practitioners.
- 7.7 The PBAC recommended that the Early Supply Rule should not apply, as it has been the PBAC's view that general nutrients be exempt.
- 7.8 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because TYR explore5 is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over TYR 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.
- 7.9 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:

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 PHENYLALANINE, TYROSINE AND SUPPLEMENTED WITH ARACHIDONIC ACID AND DOCOSAHEXAENOIC ACID					
amino acid formula with vitamins and minerals, without phenylalanine, tyrosine and supplemented with arachidonic acid and docosahexaenoic acid containing 5 g of protein equivalent powder for oral liquid, 30 x 12.5 g sachets	NEW	8	8	5	TYR explore5
Restriction Summary / Treatment of Concept:					
	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: Tyrosinaemia				

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.