

**5.14 AMINO ACID FORMULA WITH VITAMINS AND MINERALS WITHOUT METHIONINE AND SUPPLEMENTED WITH ARACHIDONIC ACID AND DOCOSAHEXAENOIC ACID,
Sachets containing oral powder 12.5 g, 30 (HCU explore5),
HCU explore5,
Vitaflo Australia Pty Ltd**

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 and supplemented with arachidonic acid (ARA) and docosahexaenoic acid (DHA) (HCU explore5) for the dietary management of pyridoxine non-responsive homocystinuria (HCU).

2 Background

- 2.1 HCU explore5 is a low volume, concentrated, methionine-free protein substitute containing 5 grams of protein equivalent (PE) per sachet for the dietary management of HCU. It is expected that HCU explore5 will largely be used to treat infants and young children from 6 months to 5 years of age.

Registration status

- 2.2 The sponsor of HCU explore5 confirmed it meets the requirements 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*.
- 2.3 As HCU 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

- 2.4 HCU explore5 has not previously been considered by the PBAC.

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

3 Requested listing

- 3.1 The submission requested HCU explore5 be listed under the same circumstances as HCU gel. The requested maximum quantity for HCU explore5 was 8 cartons, compared

to the current PBS listing of HCU gel which has a maximum quantity of 4 cartons. The maximum quantity of 8 cartons provides the same quantity of PE as the current HCU 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 METHIONINE, AND SUPPLEMENTED WITH ARACHIDONIC ACID AND DOCOSAHEXAENOIC ACID</i>					
<i>amino acid formula with vitamins and minerals without methionine 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>HCU explore5</i>
Restriction Summary [5534] / Treatment of Concept: [5534]					
Category / Program:	GENERAL – General Schedule (Code GE)				
Prescriber type:	<input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners				
PBS Indication:	Pyroxidine non-responsive homocystinuria				
Restriction Level / Method:	<input checked="" type="checkbox"/> Restricted benefit				

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

4 Comparator

4.1 The submission nominated HCU gel as the primary comparator and HCU cooler10 as the secondary comparator (as the latter contains DHA). The PBAC considered this to be an appropriate comparator and considered that the alternative comparators identified by the Nutritional Products Working Party (NPWP) for the treatment of HCU would be appropriate alternate therapies.

The NPWP identified the following alternative comparators:

- HCU Anamix infant
- HCU Anamix Junior

4.2 The PBAC noted HCU gel was previously recommended on the basis of cost minimisation (per gram of PE) to XMET Maxamaid powder, and there are many other comparators which have been cost-minimised to XMET Maxamaid powder 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 No clinical trials were presented in the submission comparing HCU explore5 to the comparators.

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 HCU explore5 are very similar in formulation and thus HCU explore5 should have the same palatability of PKU explore5. The PBAC noted PKU explore5 appears to have significant formulation differences compared with HCU 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 HCU explore5 compared with HCU gel. The submission provided a comparison of the nutritional profile of HCU explore5 with HCU gel presented as Table 1.

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

5.8 The submission also made claims throughout the main body relating to potential additional benefits of HCU 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.

Public Summary Document – March 2023 PBAC Meeting

Table 1: Nutritional composition of HCU explore5 and nominated comparator HCU gel.

Nutrient per 100 g powder	HCU explore5 (Unflavoured)	HCU gel (Unflavoured)
Energy kJ	1450	1440
kcal	342	339
Protein Equivalent g	40	41.7
L-Methionine* mg	-	0
Carbohydrate g	42	42.9
O/W sugars g	28	27.1
Fat g	1.5	0.05
O/W saturates g	0.7	0.0
O/W pufas^ g	0.5	<0.05
DHA mg	140	-
ARA mg	280	-
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 (24)	14 (31.8)
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

Public Summary Document – March 2023 PBAC Meeting

Nutrient per 100 g powder	HCU explore5 (Unflavoured)	HCU gel (Unflavoured)
Iodine mcg	150	138
Molybdenum mcg	40	50
Selenium mcg	31	35
Chromium mcg	30	71
Amino Acids (g)		
L-Alanine	1.97	2.05
L-Arginine	3.27	3.41
L-Aspartic Acid	4.37	4.56
L-Cystine	1.31	1.37
L-Glutamine	3.49	4.02
Glycine	2.87	3.00
L-Histidine	2.05	2.14
L-Isoleucine	3.08	3.21
L-Leucine	5.33	5.57
L-Lysine	3.43	3.59
L-Phenylalanine	2.38	2.48
L-Proline	3.00	3.13
L-Serine	2.30	2.40
L-Threonine	2.34	2.44
L-Tryptophan	1.03	1.07
L-Tyrosine	2.36	2.46
L-Valine	3.39	3.53
L-Carnitine (mg/100g)	44	46
Taurine (mg/100g)	88	92

Source: Appendix 1 and 2 of the submission

*No added Methionine. 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 HCU explore5 compared with HCU gel and HCU cooler 10, 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 nominated comparators

	HCU explore5	HCU gel	HCU cooler 10
Presentation	30 x 12.5 g sachets 150 g PE	30 x 24 g sachets 300 g PE	30 x 87 mL sachets 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 HCU explore5 against the comparator.
- 5.12 Table 3 presents the estimated extent of use, cost of HCU 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 HCU 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 HCU explore5 has been developed to replace HCU gel. If HCU explore5 was recommended for PBS listing the sponsor indicated it would request the delisting of HCU gel.

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 HCU explore5						
Cost to PBS/RPBS less co-payment	█ ²	█ ²	█ ²	█ ²	█ ²	█ ²
Estimated financial implications of HCU gel						
Number of scripts changed listing HCU gel	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹
Cost to PBS/RPBS less co-payment	█ ³	█ ³	█ ³	█ ³	█ ³	█ ³
Net financial implications						
Net cost to PBS/RPBS	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹	█ ¹

Source: Vitaflo HCU explore5 UCM Workbook November22

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

^a Assuming 12.167 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 HCU explore5 as a General Schedule Restricted Benefit listing for the dietary management of pyridoxine non-responsive HCU on a cost-minimisation basis to the lowest cost comparator on a price per gram of PE basis.

6.2 The NPWP advised that HCU gel was an appropriate comparator for HCU explore5, and HCU Anamix infant and HCU Anamix Junior were also alternate comparators.

6.3 The NPWP advised that HCU explore5 is nutritionally similar to the comparators and would provide a non-inferior clinical benefit.

6.4 The NPWP advised that HCU explore5 is interchangeable with the comparators at a prescribing level.

6.5 The NPWP agreed with the sponsor's estimation that listing HCU 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 HCU 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 methionine and supplemented with arachidonic acid (ARA) and docosahexaenoic acid (DHA) (HCU explore5) for the dietary management of pyridoxine non-responsive homocystinuria (HCU) under the same circumstances as HCU 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 HCU explore5 should be cost-minimised to the lowest cost comparator accepted by the NPWP (HCU gel, HCU Anamix infant or HCU Anamix Junior) at an equivalent price per gram of PE.
- 7.3 The PBAC noted and supported the NPWP advice that HCU explore5 is nutritionally similar to the comparators and would provide a non-inferior clinical benefit.
- 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 PBAC considered that HCU explore5 is interchangeable with the comparators (HCU gel, HCU Anamix infant and HCU Anamix Junior) at a prescribing level.
- 7.6 The PBAC advised that HCU 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 HCU explore5 is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over HCU 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	No. of Rpts	Available brands
AMINO ACID FORMULA WITH VITAMINS AND MINERALS WITHOUT METHIONINE, AND SUPPLEMENTED WITH ARACHIDONIC ACID AND DOCOSAHEXAENOIC ACID					
amino acid formula with vitamins and minerals without methionine 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	HCU explore5
Restriction Summary [5534] / Treatment of Concept: [5534]					
Concept ID (for internal Dept. use)	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: Pyroxidine non-responsive homocystinuria					

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.