

- 6.10 AMINO ACID FORMULA WITH VITAMINS AND MINERALS WITHOUT METHIONINE**
Sachets containing oral powder 25 g, 30 (HCU express 15)
HCU express 15
Vitaflo Australia Pty Ltd
- 6.11 AMINO ACID FORMULA WITH VITAMINS AND MINERALS WITHOUT PHENYLALANINE**
Sachets containing oral powder 34 g, 30 (PKU express 20)
PKU express 20
Vitaflo Australia Pty Ltd
- 6.12 AMINO ACID FORMULA WITH VITAMINS AND MINERALS WITHOUT PHENYLALANINE**
Sachets containing oral powder 25 g, 30 (PKU express 15)
PKU express 15
Vitaflo Australia Pty Ltd
- 6.13 AMINO ACID FORMULA WITH VITAMINS AND MINERALS WITHOUT PHENYLALANINE AND TYROSINE**
Sachets containing oral powder 25 g, 30 (TYR express 15)
TYR express 15
Vitaflo Australia Pty Ltd
- 6.14 AMINO ACID FORMULA WITH VITAMINS AND MINERALS WITHOUT VALINE, LEUCINE AND ISOLEUCINE**
Sachets containing oral powder 25 g, 30 (MSUD express 15)
MSUD express 15
Vitaflo Australia Pty Ltd

1 Purpose of Application

- 1.1 The committee secretariat submission requested HCU Express 15, PKU Express 15, PKU Express 20, TYR Express 15 and MSUD Express 15 (herein referred to Express) with new formulation continue to be listed on the Pharmaceutical Benefits Scheme (PBS).

2 Background

- 2.1 Express is indicated for patients from three years of age and is available on the PBS with Restricted Benefits for several disorders of protein metabolism.
- 2.2 PKU Express15, PKU Express20, MSUD Express15, TYR Express15, and HCU Express15 each 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 The submission did not request price changes for the new formulation of PKU Express15, PKU Express20, MSUD Express15, TYR Express15 or HCU Express15.

For more detail on PBAC's view, see section 6 PBAC outcome.

3 Requested Listing

- 3.1 The submission requested no changes to existing listings of HCU Express 15, PKU Express 15, PKU Express 20, TYR Express 15 or MSUD Express 15.

For more detail on PBAC's view, see section 6 PBAC outcome.

4 Consideration of the evidence

Sponsor hearing

- 4.1 There was no hearing for this item.

Consumer comments

- 4.2 The PBAC noted that this item received no consumer comments.

Other relevant matters

- 4.3 The submission claimed that the minor changes made to each of the five products were identical. The key differences between the current and new formulation of Express range products and the rationale behind these changes are summarised in Table 1.

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Table 1: Key nutritional changes to the Express range formulations and the rationale behind these changes.

Nutrient	Extent of change (approximate)	Sponsor's rationale
Vitamins		
Vitamin D3	+127%*	The submission did not highlight this change.
Vitamin K	-30%	Intakes in individuals with an IEM, on a restricted protein diet, may be very low, and so the aim is to provide 100% in the form of dietary supplementation. There is no evidence to support a higher requirement of Vitamin K and so a higher intake does not seem warranted.
Niacin	-60%**	Most of the niacin equivalents" (NE) within the Express range is contributed by tryptophan (See Appendix 2, 2a-c); critical to meet World Health Organisation safe protein intakes and so added niacin has been reduced.
Folate	-25%	The decrease is made so that no greater than 100% of the European Food Safety Authority (EFSA) Population Reference Intake (PRI) from dietary supplementation is to be provided.
Pathotenic Acid	-27%	The widespread occurrence of releasable pantothenic acid in food makes a dietary deficiency unlikely. Vitamin B5 content of the Express range has been set to provide 100% of WHO recommended intakes.
Minerals and Electrolytes		
Sodium	-17%	Electrolytes can be freely consumed as part of a low protein diet by individuals with PKU and other IEM and are not considered essential nutrients. These mineral decreases fall within, and comply with, Australian Food Standards concerning Food for Special Medical Purposes.
Potassium	-26%	
Chloride	-42%	
Magnesium	-12%	The content of magnesium in the Express range has been lowered to meet 100% of the EFSA's AI (adequate intake) for magnesium. This authority concluded that average requirements and PRIs could not be derived.
Trace Elements		
Zinc	-21%	High levels of zinc relative to copper can result in copper deficiency due to zinc-copper antagonism. A copper: zinc ratio of 1: 10 is recommended for optimal growth and absorption. The Express range aims to provide at least 120% NRV zinc to account for nutrient interactions, risk of zinc deficiency with low intakes, and poor zinc bioavailability and absorption from fortified sources. The zinc content of Express is in line Australian Nutrient Reference Values (NRVs) (Appendices 3-8).
Selenium	-9%	This is more consistent with Australian NRVs (Appendices 3-8).
Molybdenum	-51%	No molybdenum deficiencies have been reported within the IEM community or general population. Express provides 100% Recommended Dietary Intake (RDI) for molybdenum and is more aligned to the Australian NRVs (Appendices 3-8).
Chromium	-52%	Express provides 100% RDI for Chromium and is more aligned with NRVs (Appendices 3-8).
Manganese	-53%	AI's have been set by the Institute of Medicine (9) based upon the dietary intake of the general US population, rather than physiological requirement. The EFSA have adopted this approach and set an AI of 3mg/day based upon observed mean intakes within the EU for adolescents, adults, pregnant and lactating women (13) rather than physiological requirements.

Source: Appendix 9 of submission unless otherwise stated, * calculated by the Secretariat based on information provided in Appendix 1, **only for PKU Express 15 and PKU Express 20.

- 4.4 The key differences between the current and new formulation of Express range products were:
- decreases in the level of micronutrients including vitamin K, folate, pantoic acid, sodium, potassium, chloride, magnesium, zinc, selenium, molybdenum, chromium and manganese in all formulations
 - decreases in the level of niacin only in both PKU express.
 - increases in the level of vitamin D3 in all formulations.
- 4.5 The submission stated the formulation changes have had no effect on the properties of the Express range and have improved its vitamin, mineral, and trace element profile in line with current international nutritional recommendations, including the European Food Safety Authority's Dietary Reference Values, national standards and Australian Nutrient Reference Values.
- 4.6 The submission stated there are slight differences in the amino acid profile for MSUD Express 15, TYR Express 15 and HCU Express 15. The submission stated that this is due to an insignificant change to the addition rate of the amino acid pre-mix used and that due to the small changes in micronutrient profiles, this was essential to maintain product stability.
- 4.7 There are no changes to the amino acid profile of both PKU Express 15 and PKU Express 20.

For more detail on PBAC's view, see section 6 PBAC outcome.

5 NPWP Consideration

- 5.1 The Nutritional Products Working Party (NPWP) advised that the changes to the formulations will continue to meet the Australian adequate intake (AI) levels and recommended dietary intake (RDI) values of patients eligible for PBS subsidised use.
- 5.2 The NPWP did not have any concerns regarding the safety of these changes. The NPWP supported the continued subsidy of Express on the PBS under the existing conditions.

For more detail on PBAC's view, see section 6 PBAC outcome.

6 PBAC Outcome

- 6.1 The PBAC recommended continuing the Restricted Benefits listings of HCU Express 15, PKU Express 15, PKU Express 20, TYR Express 15 or MSUD Express 15 with new formulation under the existing conditions of the respective product.
- 6.2 The PBAC noted these new formulations are safe and will continue to meet the Australian adequate intake levels and recommended dietary intake values of patients eligible for PBS subsidised use.

- 6.3 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 No changes to the existing listing.

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the 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.