6.06 AMINO ACID FORMULA WITH VITAMINS AND MINERALS WITHOUT VALINE, LEUCINE AND ISOLEUCINE
Oral powder 400 g
MSUD Anamix Infant®
Sachets containing oral powder 36 g, 30
MSUD Anamix Junior
Oral liquid 125 mL, 30
MSUD Lophlex LQ 20
Oral powder 500 g
MSUD Maxamum
Nutricia Australia Pty Ltd

1 Purpose of Submission

1.1 The Committee Secretariat submission requested to extend the current PBS listing of maple syrup urine disease (MSUD) Anamix Infant, MSUD Anamix Junior, MSUD Lophlex LQ 20, and MSUD Maxamum to include patients diagnosed with short-chain enoyl Co-A hydratase 1 (ECHS1) deficiency (ECHS1 deficiency).

2 Background

Registration status

2.1 MSUD Anamix Infant® (PBS Code 2380G), MSUD Anamix Junior (PBS Code 10259Y), MSUD Lophlex LQ 20 (PBS Code 1546J) and MSUD Maxamum (PBS Code 8057C) are PBS listed for the dietary management of proven maple syrup urine disease (MSUD).

2.2 The proposed MSUDs are marketed as nutritional products and not therapeutic goods, they are not registered in the Australian Register of Therapeutic Goods.

Previous PBAC consideration

2.3 MSUD Anamix Infant® (PBS Code 2380G), MSUD Anamix Junior (PBS Code 10259Y), MSUD Lophlex LQ 20 (PBS Code 1546J) and MSUD Maxamum (PBS Code 8057C) have not been previously considered by the PBAC for the dietary management of ECHS1 deficiency.

3 Requested listing

3.1 The submission's proposed additions are shown with bold text and addition is bold italic text.

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 VALINE, LEUCINE AND ISOLEUCINE					
amino acid formula with vitamins and minerals without valine, leucine and isoleucine powder for oral liquid, 400 g	2380G MP NP	8	8	5	MSUD Anamix Infant
amino acid formula with vitamins and minerals without valine, leucine and isoleucine oral liquid: powder for, 30 x 36 g sachets	10259Y MP NP	4	4	5	MSUD Anamix Junior
amino acid formula with vitamins and minerals without valine, leucine and isoleucine oral liquid, 30 x 125 mL pouches	1546J MP NP	3	3	5	MSUD Lophlex LQ 20
amino acid formula with vitamins and minerals without valine, leucine and isoleucine powder for oral liquid, 500 g	8057C MP NP	8	8	5	MSUD Maxamum
Restriction Summary / Treatment of Concept					
	Category / Program: ☒ GENERAL - General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners ☒Nurse Practitioners				
	Restriction type: ☒Restricted Benefit				
	Indications: Maple syrup urine disease				
Restriction Summary / Treatment of Concept					
	Category / Program: ☒ *GENERAL - General Schedule (Code GE)*				
	Prescriber type: ☒*Medical Practitioners* ☒*Nurse Practitioners*				
	Restriction type: ☒*Restricted Benefit*				
	Indication: *Short-chain enoyl Co-A hydratase1 (ECHS1) deficiency*				

3.2 The submission proposed no change to the maximum quantity and number of repeats of MSUD products on the PBS when used for ECHS1 deficiency indication. The maximum quantity and number of repeats provide supply for approximately 6 months of therapy.

4 Consideration of the evidence

Sponsor hearing

4.1 There was no hearing for this item.

Consumer input

4.2 The PBAC noted and welcomed input received via the Office of Health Technology Assessment Consultation Hub from the Mito Foundation. The input supported the proposed extension of the PBS listings for MSUD products to include the dietary management of ECHS1 deficiency. The PBAC noted that the proposed extension would improve access to clinically recommended dietary therapy for patients with these rare metabolic disorders.

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

4.3 The submission described ECHS1 deficiency as an ultra rare inherited mitochondrial disorder of valine metabolism that causes accumulation of toxic metabolites, leading to severe and rapidly progressive neurological disease, with early death if untreated. There is no drug therapy for the underlying metabolic defect; the only disease modifying treatment is early, long term dietary restriction of valine and leucine, similar to the approach used in maple syrup urine disease (MSUD).

4.4 The submission stated patients require nutritionally complete medical formulas that are leucine-free and extremely low in valine. The submission argued that existing MSUD products listed on the PBS meet these requirements and are the only suitable options available in Australia. No alternative PBS-listed products exist for dietary management of ECHS1 deficiency.

4.5 The submission stated International and Australian clinical experience indicates that MSUD formulas are already standard care for ECHS1 deficiency and are associated with biochemical stabilisation and slowed or improved neurological outcomes. The submission stated there are no changes to MSUD product formulations, and the products have an established safety profile.

Equity and Access Considerations

4.6 The submission considered that current PBS restrictions significantly limit access to essential specialised medical nutrition. As a result, families of children with ECHS1 deficiency are forced to rely on hospital discretionary funding, short-term compassionate supply arrangements, or full out-of-pocket payment.

4.7 Clinician correspondence included in the submission (for example, from the Royal Melbourne Hospital) indicated that institutional reluctance to assume ongoing costs has already delayed access to this essential nutrition for patients. Such delays or interruptions in treatment are associated with irreversible neurological injury, metabolic crises requiring intensive care admission, and preventable early mortality.

Cost and Estimated PBS usage and financial implications

4.8 The submission proposed no change to current prices of MSUD products for extending the indication to include ECHS1 deficiency (Table 1). The current prices of MSUD products for currently PBS indication are listed in below table.

Table 1: current prices of MSUD products for maple syrup urine disease on the PBS proposed for ECHS1 deficiency

Product	PBS Code	Max. qty units	№.of Rpts	AEMP	DPMQ
MSUD Anamix Infant®	2380G	8	5	$[redacted]	$634.40
MSUD Anamix Junior®	10259Y	4	5	$[redacted]	$1,744.12
MSUD Lophlex LQ 20	1546J	3	3	$[redacted]	$2,560.68
MSUD Maxamum	8057C	8	5	$[redacted]	$2,241.04

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

4.9 Table 2 presents the estimated extent of use, cost of MSUD products 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.

4.10 In the provided UCM workbook, the Secretariat noted that the sponsor has provided input for both number of script proposed and scripts affected. The Secretariat considers the input for the scripts affected is not necessary as this market has been captured in the number of scripts proposed worksheet leading to double counting and an overestimation in the net impact by 2-fold. The information in this worksheet has been removed. Table 2 below shows the resulting net impact, with the sponsor's current estimates and the Secretariat's amendments. On this basis, the Secretariat considered that the estimated net financial impact to the PBS/RPBS for listing MSUD products should be $0 to < $10 million over six years, rather than $0 to < $10 million (Year 1: $0 to < $10 million instead of $0 to < $10 million; Year 6: $0 to < $10 million instead of $0 to < $10 million).

Table 2: Estimated use and financial implications of MSUD Anamix Infant, MSUD Anamix Junior, MSUD Lophlex LQ and MSUD Maxamum

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Total all patients with ECHS1	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Estimated extent of use - Number of scripts dispensed						
MSUD Anamix Infant	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
MSUD Anamix Junior	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
MSUD Lophlex LQ	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
MSUD Maxamum	[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]
Estimated aggregate financial implications of MSUD Anamix Infant, MSUD Anamix Junior, MSUD Lophlex LQ and MSUD Maxamum						
New listing Cost to PBS/RPBS less co-payment ($)	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Changed listing Cost to PBS/RPBS less co-payment ($)	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Net financial implications – sponsor's estimation (overestimation)						
Net cost to PBS/RPBS ($)	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Net financial implications – PBAC Secretariat's estimation (amendment)						
Net cost to PBS/RPBS ($)	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]

Abbreviations: PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme.
The redacted values correspond to the following ranges:
[1] *< 500*
[2] *$0 to < $10 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 PBS-listed maple syrup urine disease MSUD products to the management of mitochondrial enoyl-coA hydratase, short chain 1 deficiency (ECHS1) deficiency.

5.2 The NPWP advised that it considers MSUD products clinically appropriate for ECHS1 deficiency, given the shared need for valine restriction, the absence of products without valine alone in Australia, and current Australian and international practice.

5.3 The NPWP advised that children receiving MSUD products for ECHS1 deficiency may need leucine and isoleucine supplementation, which should be monitored and managed by clinicians. The NPWP stated this supplementation can be achieved through breast milk or natural protein food sources, with supplements only if necessary.

5.4 The NPWP advised that the current maximum quantity and repeats are appropriate for ECHS1 deficiency.

5.5 The NPWP advised that the existing PBS safety profile of MSUD products can reasonably be extrapolated to ECHS1 deficiency, with no additional risk management needed.

5.6 The NPWP noted that in submission items 6.07 and 6.08 it had supported extending the listing of amino acid formulas with vitamins and minerals without valine, leucine and isoleucine (MSUD express 15® and MSUD Explore5) to include ECHS1 and 3-hydroxyisobutyryl-CoA hydrolase (HIBCH) deficiencies. For consistency, the NPWP advised that the proposed extension for MSUD Anamix Infant®, MSUD Anamix Junior®, MSUD Lophlex LQ 20®, MSUD Maxamum® should also include the management of HIBCH deficiency.

6 PBAC Outcome

6.1 The PBAC recommended amending the current General Schedule Restricted Benefit listings for MSUD Anamix Infant, MSUD Anamix Junior, MSUD Lophlex LQ 20 and MSUD Maxamum to include patients diagnosed short-chain enoyl Co-A hydratase 1 (ECHS1) deficiency (ECHS1 deficiency).

6.2 The PBAC noted that the NPWP had supported extending the use of PBS-listed MSUD products to include the dietary management of HIBCH deficiency, in addition to ECHS1 deficiency. The PBAC also noted its recommendation to extend the listings of amino acid formulas with vitamins and minerals without valine, leucine and isoleucine (MSUD Express 15® and MSUD Explore 5®) to include patients with ECHS1 and HIBCH deficiencies. For consistency, the PBAC advised that the proposed extension to the listings for MSUD Anamix Infant®, MSUD Anamix Junior®, MSUD Lophlex LQ 20® and MSUD Maxamum® should also include the dietary management of HIBCH deficiency, including permitting prescribing by both medical practitioners and nurse practitioners. The PBAC also noted that the proposed maximum quantities and repeats for the MSUD products are appropriate.

6.3 The PBAC recommended no change to the current price of MSUD Anamix Infant, MSUD Anamix Junior, MSUD Lophlex LQ 20 and MSUD Maxamum for the proposed extension to include dietary management of ECHS1 and HIBCH deficiencies.

6.4 The PBAC noted the NPWP advice that children receiving MSUD products for ECHS1 deficiency may need leucine and isoleucine supplementation, which should be monitored and managed by clinicians. The PBAC also noted the NPWP stated this supplementation can be achieved through breast milk or natural protein food sources, with supplements only if necessary.

6.5 The PBAC considered the Secretariat's estimate of the financial implications to be appropriate.

6.6 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 of maple syrup urine disease (MSUD) Anamix Infant, MSUD Anamix Junior, MSUD Lophlex LQ 20, and MSUD Maxamum to include patients diagnosed with ECHS1 and HIBCH deficiencies.is not expected to address a high and urgent unmet clinical need.

6.7 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 Amend existing listing as follows:

Add new indications to **MSUD Anamix Infant** and **MSUD Maxamum** 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 VALINE, LEUCINE AND ISOLEUCINE					
amino acid formula with vitamins and minerals without valine, leucine and isoleucine powder for oral liquid, 400 g	2380G MP NP	8	8	5	MSUD Anamix Infant
amino acid formula with vitamins and minerals without valine, leucine and isoleucine powder for oral liquid, 500 g	8057C MP NP	8	8	5	MSUD Maxamum
Restriction Summary / Treatment of Concept					
	Category / Program: ☒ GENERAL - General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners ☒Nurse Practitioners				
	Restriction type: ☒Restricted Benefit				
	Indication: Short-chain enoyl Co-A hydratase 1 (ECHS1) deficiency				

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 VALINE, LEUCINE AND ISOLEUCINE					
amino acid formula with vitamins and minerals without valine, leucine and isoleucine powder for oral liquid, 400 g	2380G MP NP	8	8	5	MSUD Anamix infant
amino acid formula with vitamins and minerals without valine, leucine and isoleucine powder for oral liquid, 500 g	8057C MP NP	8	8	5	MSUD Maxamum

Restriction Summary / Treatment of Concept	
	Category / Program: ☒ GENERAL - General Schedule (Code GE)
	Prescriber type: ☒Medical Practitioners ☒Nurse Practitioners
	Restriction type: ☒Restricted Benefit
	Indication: 3-hydroxyisobutyryl Co-A hydrolase (HIBCH) deficiency

Add new indications to **MSUD 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 VALINE, LEUCINE AND ISOLEUCINE					
amino acid formula with vitamins and minerals without valine, leucine and isoleucine oral liquid: powder for, 30 x 36 g sachets	10259Y MP NP	4	4	5	MSUD Anamix Junior
Restriction Summary / Treatment of Concept					
	Category / Program: ☒ GENERAL - General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners ☒Nurse Practitioners				
	Restriction type: ☒Restricted Benefit				
	Indication: Short-chain enoyl Co-A hydratase 1 (ECHS1) deficiency				

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 VALINE, LEUCINE AND ISOLEUCINE					
amino acid formula with vitamins and minerals without valine, leucine and isoleucine oral liquid: powder for, 30 x 36 g sachets	10259Y MP NP	4	4	5	MSUD Anamix Junior
Restriction Summary / Treatment of Concept					
	Category / Program: ☒ GENERAL - General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners ☒Nurse Practitioners				
	Restriction type: ☒Restricted Benefit				
	Indication: 3-hydroxyisobutyryl Co-A hydrolase (HIBCH) deficiency				

Add new indications to **MSUD Lophlex LQ 20** 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 VALINE, LEUCINE AND ISOLEUCINE					

amino acid formula with vitamins and minerals without valine, leucine and isoleucine oral liquid, 30 x 125 mL pouches	1546J MP NP	3	3	5	MSUD Lophlex LQ 20
Restriction Summary / Treatment of Concept					
	Category / Program: ☒ GENERAL - General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners ☒Nurse Practitioners				
	Restriction type: ☒Restricted Benefit				
	Indications: Short-chain enoyl Co-A hydratase 1 (ECHS1) deficiency				

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 VALINE, LEUCINE AND ISOLEUCINE					
amino acid formula with vitamins and minerals without valine, leucine and isoleucine oral liquid, 30 x 125 mL pouches	1546J MP NP	3	3	5	MSUD Lophlex LQ 20
Restriction Summary / Treatment of Concept					
	Category / Program: ☒ GENERAL - General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners ☒Nurse Practitioners				
	Restriction type: ☒Restricted Benefit				
	Indication: 3-hydroxyisobutyryl Co-A hydrolase (HIBCH) deficiency				

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.