6.16 TRIGLYCERIDES MEDIUM CHAIN FORMULA
Oral powder 400 g,
Peptamen Junior®,
Nestle Health Science

1 Purpose of Application

1.1 The minor submission requested a Restricted Benefit listing of a triglycerides medium chain formula, Peptamen Junior®, for the dietary management of malnutrition and/or intolerance to conventional enteral nutrition formulas for critically or chronically ill paediatric patients who are dependent on nutritional therapy due to short bowel syndrome, neurological impairment (e.g. cerebral palsy), cystic fibrosis, Crohn's disease, malabsorption, chronic diarrhoea, HIV/AIDS, burns and cancer.

2 Background

2.1 Peptamen Junior is currently listed on the PBS for fat malabsorption due to liver disease, short gut syndrome, cystic fibrosis and gastrointestinal disorders.

2.2 In the minor submission, the sponsor confirmed that Peptamen Junior 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.*

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

3 Requested listing

3.1 The submission requested the following new listing.

3.2 Suggestions and additions proposed by the Secretariat to the requested listing are added in italics and suggested deletions are crossed out with strikethrough.

Name, Restriction, Manner of administration and form	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Proprietary Name and Manufacturer	
TRIGLYCERIDES MEDIUM CHAIN FORMULA oral powder 400 g	NEW	8	8	5	Peptamen Junior®	Nestle Health Science

Restriction Summary [new] / Treatment of Concept: [new]

Concept ID	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: ☐Dental ☒Medical Practitioners ☒Nurse practitioners ☐Optometrists ☐Midwives
	Restriction Level / Method: ☐Unrestricted benefit ☒Restricted benefit ☐Authority Required – In Writing ☐Authority Required – Telephone/Electronic/Emergency ☐Authority Required – Streamlined

	Condition: *Malnutrition and/or intolerance to conventional enteral nutrition formulas*
NEW	**Indication:** *Dietary management of malnutrition and/or intolerance to conventional enteral nutrition formulas for critically or chronically ill paediatric patients aged 1 to 10 years, who are dependent on nutritional support therapy*
	Clinical criteria:
NEW	*Patient must have malnutrition caused by short bowel syndrome*
	OR
	Clinical criteria:
NEW	*Patient must have malnutrition caused by neurological impairment*
	OR
	Clinical criteria:
NEW	*Patient must have malnutrition caused by cystic fibrosis*
	OR
	Clinical criteria:
NEW	*Patient must have malnutrition caused by Crohn's disease*
	OR
	Clinical criteria:
NEW	*Patient must have malnutrition caused by malabsorption*
	OR
	Clinical criteria:
NEW	*Patient must have malnutrition caused by chronic diarrhoea*
	OR
	Clinical criteria:
NEW	*Patient must have malnutrition caused by HIV/AIDS*
	OR
	Clinical criteria:
NEW	*Patient must have malnutrition caused by burns*
	OR
	Clinical criteria:
NEW	*Patient must have malnutrition caused by cancer*

NPWP advice on requested listing and population

3.3 The NPWP noted the request for an additional PBS listing for Peptamen Junior for the dietary management of malnutrition and/or intolerance to conventional enteral nutrition formulas for critically or chronically ill paediatric patients who are dependent on nutritional therapy due to short bowel syndrome, neurological impairment (e.g. cerebral palsy), cystic fibrosis, Crohn's disease, malabsorption, chronic diarrhoea, HIV/AIDS, burns and cancer.

3.4 The NPWP considered that the proposed population was not well defined and that it would be difficult to determine which patients could be considered 'critically or chronically ill'. The NPWP was concerned that this could lead to inappropriate use and a large cost to the PBS.

3.5 The Sponsor adjusted the wording of the indication in the pre-PBAC response to 'For the dietary management of malnutrition **and** intolerance to conventional enteral nutrition formulas for critically or chronically ill paediatric patients who are dependent on nutritional therapy due to short bowel syndrome, neurological impairment (e.g.

cerebral palsy), cystic fibrosis, Crohn's disease, malabsorption, chronic diarrhoea, HIV/AIDS, burns and cancer.'

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

4 Comparator

4.1 The submission stated that there were no comparators currently PBS listed for the requested indication. The submission nominated Peptamen Junior used in the private market as the comparator. However, the submission did list a number of enteral nutrition products that had been approved for use in Queensland Health public hospitals and institutions, as assessed by the Queensland Health Medicines Advisory Committee (QHMAC), with advice from the Nutrition Subcommittee (NUSCo). These products include Fortini®, Neocate Junior®, Nutrini Peptisorb®, Nutrini Peptisorb Energy®, Peptamen Junior®, PediaSure®, and Ketocal®. Nutrini Peptisorb, Nutrini Peptisorb Energy and Peptamen Junior are all PBS listed for 'dietary management of conditions requiring a source of medium chain triglycerides', Neocate Junior is PBS listed for 'severe intestinal malabsorption including short bowel syndrome', and Ketocal is PBS listed for a 'ketogenic diet'.

4.2 The pre-PBAC response argued that not all patients have access to cost neutral supply through hospitals as they could be located in rural or remote settings, and delivery or travel and accommodation could be costly.

NPWP advice on comparator

4.3 The NPWP considered that standard enteral nutrition products, such as Ensure or PediaSure, were the appropriate comparators. The NPWP noted that these products are available through hospital programs on a cost neutral basis to patients and families (i.e. at the cost of regular diet), and that these mechanisms were effective and equitable. The NPWP also considered that the majority of patients tolerate standard enteral formulas, and there was no clear evidence presented in the minor submission to show that Peptamen Junior was superior to standard enteral nutrition. The NPWP also considered that patients who are intolerant to standard enteral formula were adequately managed through current PBS arrangements.

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

5 Consideration of the evidence

Sponsor hearing

5.1 There was no hearing for this item as it was a minor submission.

Consumer comments

5.2 The PBAC noted that no consumer comments were received for this item.

Clinical trials

5.3 The submission presented a number of clinical trials to support the use of Peptamen Junior for the proposed PBS indication. Details of the trials are provided in Table 1.

Table 1: Trials and associated reports presented in the submission

Indication relevant to proposed PBS listing	Citation	Study design	Study population	Intervention and duration	Key results
Crohn's disease	Polk DB. Hattner JAT, 1992	1-year prospective study	6 children with Crohn's disease	100% whey peptide formula with MCTs by nocturnal nasogastric infusion at a caloric equivalent of 50th percentile for age, as the exclusive nutrient source 1 out of 4 months during a 1-year period	In a cohort of six children with Crohn's disease and growth failure (height <5th percentile), intermittent supplemental feeding with 100% whey peptide formula with MCTs followed by an exclusion diet for 12 months resulted in significant improvements in height (height velocity accelerated from 2.6 ±0.8 to 9.3±0. cm/year; p<0.0001) and weight (weight velocity increased from 3.0±1.2 to 6.63±1.2 kg/year; p<0.02) from baseline.
Gastrointestinal dysmotility, Crohn's disease, short bowel syndrome	Vikram Khoshoo, Sun, & Storm, 2010	6-week randomised, double-blind, crossover study	12 children with gastrointestinal dysmotility (n=9), Crohn's disease (n=3), or mild short bowel syndrome (n=2)	Children received one of two formulas for 2 weeks followed by a 5-day washout period and then the second diet for another 2 weeks: • A 100% whey, peptide-based formula without fibre (control) • A 100% whey, peptide-based formula with fibre and prebiotic During the run-in and washout periods, participants were fed the fibre-free formula, Peptamen Junior, similar to the control formula used.	Feeding with Peptamen Junior with added fibre was associated with improved stool consistency, decreased abdominal distension, and decreased flatulence compared with when the same formula without fibre was administered. No significant differences were observed in vomiting, abdominal pain, feeding intake, or weight gain between the two formulas. This study showed that Peptamen Junior was as well tolerated as a peptide-based formula containing fibre in a small population of children with gastrointestinal impairments.

Indication relevant to proposed PBS listing	Citation	Study design	Study population	Intervention and duration	Key results
Short bowel syndrome, neurological impairment, cystic fibrosis, cancer and other conditions associated with malabsorption	Leonard et al., 2019	Retrospective multicentre survey on a cohort of patients between 2010 and 2015 in 12 tertiary paediatric French centres	136 children with digestive tract disease (including short bowel syndrome), neurological impairment, cystic fibrosis, haematological/oncological disease, cholestasis, ear, nose, and throat disease or unsafe to swallow, respiratory failure, heart disease and/or other pathology	Patients received a large amount of their daily caloric intake in the form of Peptamen Junior between 2010 and 2015	Body mass index improved or remained normal in 88.3% of children. Home enteral nutrition with Peptamen Junior was well tolerated and efficient in children with complex diseases featuring malabsorption and/or after failure of polymeric diet

Indication relevant to proposed PBS listing	Citation	Study design	Study population	Intervention and duration	Key results
Cancer	Hu Qun, Sun Y. Effects of a Peptide-Based Enteral Formula on Tolerance to Chemotherapy in Children with ALL Receiving an L-ASP Containing Combination Regimen. WCPGHAN 2012, November 14-18 Taipei, Taiwan (Poster).	Cohort study	Paediatric patients with acute lymphoblastic leukaemia (ALL)	Peptamen Junior duration	In a cohort of paediatric patients with ALL (n=54), dietary supplementation with Peptamen Junior (n=36) was associated with improved tolerance to chemotherapy compared with non-supplemented controls (n=18), as indicated by: • A significantly smaller decrease in blood serum albumin following chemotherapy versus control patients (serum albumin levels after chemotherapy: 35.26 g/L ± 3.62 versus 31.07 g/L ± 3.32, respectively; t=4.091; p<0.05). • A significantly better blood coagulation profile following chemotherapy versus control patients, measured by prothrombin times and activated partial thromboplastin time: - Prothrombin time: 11.47 s ± 1.75 versus 13.23 s ± 1.98, respectively (t=3.135; p<0.05) - Activated partial thromboplastin time: 32.81 s ± 7.12 versus 47.68 s ± 14.37, respectively (t=3.995; p<0.05) • A significantly higher absolute neutrophil count following chemotherapy versus control patients (1.20 ± 1.15 versus 0.50 ± 0.79, respectively; p<0.05). • A significantly shorter time to neutrophil recovery versus control patients (4.18 days ± 2.92 versus 7.29 days ± 2.16; p<0.05).

Indication relevant to proposed PBS listing	Citation	Study design	Study population	Intervention and duration	Key results
HIV/AIDS	Hampsey J, Sleasman J and Borum P. Nutrition intervention with HIV infected children. *The FASEB Journal*, 1997;11(3):A187 (Abstract presented at: Environmental Biology 1997, April 6-9, New Orleans, USA)			Yes	Intervention study enrolling 10 symptomatic HIV-infected children. Weight gain was significantly greater during six months of dietary supplementation with Peptamen Junior than in an equal time period before the study. Supplementation with Peptamen Junior also resulted in significantly increased triceps skinfold from baseline (p=0.021). Furthermore, children who consumed Peptamen Junior daily for ≥65% of the time throughout the study increased to or maintained a haematocrit of 35%, whereas those who were less compliant did not.
Chronic diarrhoea	Flack S, Lawson M, 2003)	Prospective study	15 children with eosinophilic enteropathy or food intolerance of unknown aetiology	Subjects were established on Peptamen Junior over 4 days and were reviewed after 28 days	Peptamen Junior was associated with improvement in diarrhoea, vomiting and abdominal pain. Seven of eight children (88%) with diarrhoea improved, three of three children (100%) with vomiting improved and five of six children (83%) with abdominal pain improved during the 28-day trial period. It was concluded that Peptamen Junior is well accepted and tolerated and provides a more suitable nutrient profile than existing products designed for adults or infants.

Indication relevant to proposed PBS listing	Citation	Study design	Study population	Intervention and duration	Key results
Neurological impairment (e.g. cerebral palsy)	Minor, Ochoa, Storm, & Periman, 2016)	Retrospective chart review	13 children with developmental delays who were failing to reach adequate nutritional goals on standard polymeric formulas	Patients were switched from an intact polymeric formula to one of the following peptide-based, 100% whey formulas for a minimum of 2 weeks: • Peptamen Junior (n=6) • Peptamen Junior 1.5 (n=6) • Peptamen Junior Prebio (n=1)	This retrospective study of 13 children with developmental delays evaluated the effects of switching children with developmental delays who were experiencing feeding intolerance from intact protein containing formulas to a 100% whey peptide-based formula. Of the 13 subjects assessed, 92% had improved feeding tolerance, and 75% of these reported the time to improvement within one week after formula switch. Feeding tolerance parameters that improved were vomiting (86%). Gagging and retching (75%), high residual volumes (63%), constipation (43%), diarrhoea (100%), and poor weight gain (100%). In addition, 71% of the patients tolerated increased feeding volumes. Changing to Peptamen Junior from intake protein formula improved multiple symptoms of feeding intolerance in the majority of these developmentally delayed children.

Source: Table 2.2: Summary of clinical evidence for Peptamen Junior in proposed PBS indication, pg. 31 of the submission.

5.4 The submission also presented seven studies that the sponsor claimed provided evidence in support of the effectiveness of some of highlighted the key features of the Peptamen Junior formulation (Peptamen Junior minor submission, table 2.3, page 35). These studies were not conducted using Peptamen Junior and have not been summarised here.

NPWP advice on clinical evidence

5.5 The NPWP considered that there was inadequate evidence provided in the minor submission to support broadening the current listing. The NPWP noted that the defining characteristic of Peptamen Junior is its medium chain triglycerides (MCT) component and recalled that patients who have a MCT deficiency due to short gut syndrome, Crohn's disease and chronic diarrhoea are already able to access Peptamen Junior through its current PBS listing.

Economic evaluation

5.6 The submission requested the same AEMP as Peptamen Junior on the private market and the current PBS listing for Peptamen Junior, of $36.55 per 400 g tin.

5.7 The submission claimed that it used a conservative approach regarding the duration of treatment, with Peptamen Junior being used as a sole source of nutrition for 2 months, then being used as 1 meal per day (one third of nutrition) for 2 months. The minor submission stated that this was consistent with therapeutic guidelines for paediatric Crohn's disease that recommends 6-8 weeks of exclusive enteral nutrition to induce remission.

5.8 The estimated cost for the treatment was calculated by the submission for its use as a sole source of nutrition as well as for a maintenance dose and is presented in Table 2 and Table 3. The submission used the average dose for the population aged 1-10 years of 1340.82 kcal (Table 3.1, page 42, Peptamen Junior minor submission).

Table 2: Calculation of mean treatment cost when used as a sole source of nutritional needs

Sole source of nutrition	Tins
Average daily requirement	0.72
Per week	5.05
Per month (28 days)	20.18
Total cost per month (ex-manufacturer price)	$737.74

Source: Table 3.2, Peptamen Junior minor submission, pg. 42

Table 3: Calculation of mean treatment cost when used as a maintenance dose (one-third of daily needs)

Maintenance dose	Tins
Maintenance dose per day	0.24
Per week	1.68
Per month (28 days)	6.73
Total cost per month (ex-manufacturer price)	$245.91

Source: Table 3.3, Peptamen Junior minor submission, page 43

Estimated PBS usage & financial implications

5.9 The submission estimated the number of patients treated by using the prevalence data on the paediatric malnutrition population from the World Health Organisation (WHO) and assumed that 5% of this population were severely or chronically malnourished. Of this population, the submission estimated the uptake rate would be 35% in the first year, which resulted in an estimate of less than 10,000 children receiving treatment in Year 1 (Peptamen Junior Minor Submission, page 46). Table 4 provides further details of the estimated number of scripts of Peptamen Junior likely to be dispensed in the first six years of listing across the two phases (sole source of nutrition and maintenance dosing).

Table 4: PBS script volumes for Peptamen Junior (at maximum quantity of 8)

Drug / molecule	2020	2021	2022	2023	2024	2025
PEPTAMEN® Junior as sole source of nutrition	[redacted]					
PEPTAMEN® Junior as maintenance dose	[redacted]					
Aggregate volumes	[redacted]					

Source: Table 4.5, Peptamen Junior minor submission, page 49

The redacted table shows that at Year 6, the estimated total number of scripts was less than 10,000.

5.10 The minor submission estimated a net cost to the PBS of less than $10 million in Year 6 of listing, with a total net cost to the PBS of less than $10 million over the first 6 years of listing. This is summarised in Table 5 with the expected patient and prescription numbers.

5.11 The submission stated that the listing would not have any impact on any current PBS listing, as it will be the first product to be listed for this indication.

Table 5: 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	[redacted]					
Number of scripts dispensed[a]	[redacted]					
Estimated financial implications of Peptamen Junior						
Cost to PBS/RPBS	$[redacted]					
Copayments	$[redacted]					
Cost to PBS/RPBS less copayments	$[redacted]					
Net cost to {PBS/RPBS/MBS/DHS}	$[redacted]					

[a] Assuming 693-739 per year as estimated by the submission.

Sources: Table 4.4: Number of patients electing treatment, page 49 of the submission. Table 4.5: PBS script volumes for Peptamen Junior (at maximum quantity of 8), page 49 of the submission. Table 4.7: Net cost to PBS for Peptamen Junior, page 50 of the submission.

5.12 As a minor submission, the financial estimates have not been independently evaluated.

NPWP advice to PBAC

5.13 The NPWP did not support the Restricted Benefit listing of Peptamen Junior for the dietary management of malnutrition and/or intolerance to conventional enteral nutrition formulas for critically or chronically ill paediatric patients who are dependent on nutritional therapy due to short bowel syndrome, neurological impairment (e.g. cerebral palsy), cystic fibrosis, Crohn's disease, malabsorption, chronic diarrhoea, HIV/AIDS, burns and cancer. The NPWP considered that the minor submission had failed to identify the appropriate comparator, to adequately define its target population or to demonstrate that there was a clinical need to list Peptamen Junior on the PBS for the proposed indications.

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

6 PBAC Outcome

6.1 The PBAC did not recommend the restricted benefit listing of triglycerides medium chain formula (Peptamen Junior) for the dietary management of malnutrition and intolerance to conventional enteral nutrition formulas for critically or chronically ill paediatric patients who are dependent on nutritional therapy due to short bowel syndrome, neurological impairment (e.g. cerebral palsy), cystic fibrosis, Crohn's disease, malabsorption, chronic diarrhoea, HIV/AIDS, burns and cancer. The PBAC considered that the population was poorly defined and that the submission had nominated an incorrect comparator and failed to demonstrate a clinical need for the proposed listing.

6.2 The PBAC noted that the Sponsor's pre-PBAC response had adjusted the wording of the indication (see paragraph 3.5), but agreed with the NPWP that the population was poorly defined, and considered that this could lead to inappropriate prescribing and an increased cost to the PBS.

6.3 The PBAC noted the NPWP considered the nominated comparator to be inappropriate, and considered that the comparators nominated by the NPWP, PediaSure and Ensure, were appropriate.

6.4 The PBAC noted that the pre-PBAC response argued that not all patients have access to cost neutral supply through hospitals (see paragraph 4.2), but agreed with the NPWP that the defining characteristic of Peptamen Junior is its MCT content, and that the majority of patients who required MCT or were intolerant to standard enteral nutrition were adequately managed through current PBS listings. The PBAC also agreed with the NPWP that there was inadequate evidence provided in the minor submission to support broadening the PBS listing.

6.5 The PBAC noted that this submission is eligible for Independent Review.

Outcome:

Rejected

7 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.

8 Sponsor's Comment

The sponsor had no comment.