

5.21 GLYCOMACROPEPTIDE and ESSENTIAL AMINO ACIDS
Oral liquid: powder for, 60 × 20 g sachets
PKU Restore[®],
Cortex Health Pty Ltd.

1 Purpose of Application

1.1 The minor submission requested a Restricted Benefit listing for the treatment of phenylketonuria (PKU).

2 Requested Listing

2.1 The submission requested the following new listing:

2.2 No changes to the proposed listing were suggested by the Secretariat

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
GLYCOMACROPEPTIDE and ESSENTIAL AMINO ACIDS Oral liquid: powder for, 60 × 20 g sachets	5	5	PKU Restore [®]	Cortex Health Pty Ltd

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Condition:	Phenylketonuria
PBS Indication:	Phenylketonuria
Restriction Level / Method:	<input checked="" type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <input type="checkbox"/> Authority Required – Emergency <input type="checkbox"/> Authority Required - Electronic <input type="checkbox"/> Streamlined

3 Background

3.1 The sponsor of PKU Restore[®] confirmed that it meets the requirements for foods that have medical purposes as set out under *The Australia New Zealand Food Standards Code — Standard 2.9.5: Food for Special Medical Purposes*.

3.2 The product is a different form of similar PBS-listed PKU products; PKU Restore[®] are powder sachets that can be diluted into different strengths, whereas PKU Glytactin RTD 10[®] and Camino Pro Restore[®] are pre-diluted oral liquids in bottles or cartons.

- 3.3 PKU Restore[®] contains 5 g protein equivalent (PE), while Camino Pro Restore[®] contains 10 g PE. The sponsor claimed that the lower PE provides dosing flexibility to patients, as multiple sachets can be used for a single serving.
- 3.4 PKU Restore[®] does not contain added vitamins or minerals, and the sponsor proposed that clinicians will use the product as a supplement rather than a singular source of protein for PKU patients.
- 3.5 The sponsor stated that, once their own product Camino Pro Restore[®] is delisted from the PBS and discontinued, PKU Restore[®] will serve as the only isotonic hydration-style treatment for PKU patients.
- 3.6 PKU Restore[®] has not been considered by the PBAC previously.

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

4 Comparator

- 4.1 The sponsor nominated Camino Pro Restore[®] as the main comparator. The product is also a glycomacropeptide (GMP) with essential amino acids oral liquid, for the use in children aged 2 years or older. The key differences were that PKU Restore[®] is a powder sachet, which could be more convenient to store and adjustable in strength than the pre-diluted Camino Pro Restore[®] 500mL bottles.
- 4.2 The sponsor stated that Camino Pro Restore[®] will be PBS delisted and discontinued, so a second comparator, PKU Glytactin RTD 10[®], was nominated. PKU Glytactin RTD 10[®] is a GMP oral liquid but, unlike PKU Restore[®] and Camino Pro Restore[®], does contain added vitamins and minerals and is a nutritionally complete formula.
- 4.3 The requested maximum quantity of 60 × 20 g sachets × 5 (to give a total of 1,500 g Protein Equivalent (PE)) with 5 repeats is consistent with other similar PBS-listed isotonic, hydration style drink products. Camino Pro Restore[®] is currently PBS listed at 12 × 500 mL bottles × 12 (to give a total of 1,440 g PE) with 5 repeats.

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 minor submission presented the following clinical trial:

Table 1: Trials and associated reports noted in the submission

Trial ID	Protocol title/ Publication title	Publication citation
Direct randomised trials		
	Ney, D.M.; Stroup, B.M.; Clayton, M.K.; Murali, S.G.; Rice, G.M.; Rohr, F.; and Levy, H.L., Glycomacropeptide for nutritional management of phenylketonuria: a randomised, controlled, crossover trial	The American Journal of Clinical Nutrition. 2016; 104(2):334-45

Source: Ney 2016 Clinical Trial. Compiled during the minor overview

5.4 The aim of the study was to investigate the efficacy of a low-phenylalanine diet in combination with glycomacropeptide medicinal foods (GMP-MFs) or amino acid medicinal foods (AA-MFs). The study found that treatment compliance was more likely to be higher in patients who were given GMP-MFs, compared to AA-MFs. The researchers suggested that the increased compliance may be due to the convenient packaging of GMP products, whereas AA-MFs required measurement and mixing. Blood phenylalanine concentrations were not significantly different across the treatments. GMP-MF patients noted improved gastrointestinal symptoms and decreased hunger on the treatment.

5.5 In consideration of the submission, the Nutritional Products Working Party (NPWP) noted that:

- The proposed listing was clinically and nutritionally appropriate, with suitable restriction criteria.
- The proposed comparator, Camino Pro Restore[®] was considered suitable.
- There was a clinical advantage in listing the product, as an alternative PKU brand for patients would increase the flexibility and compliance of sourcing adequate amounts of protein from various formulations.
- The product contained phenylalanine at 9 mg per 20 g sachet, which raised concern to the NPWP. However, they stated that they had no clinical indications of safety concerns over this amount of phenylalanine being present in the product being detected in blood levels.
- The product is likely to be used in combination with other PKU treatments. Therefore, the NPWP noted that the requested MQ may lead to wastage through products passing the expiry date before consumption. However, it was indicated that doctors usually prescribe ½ scripts due to wastage concerns.
- Concern was raised over the recent increase in the listing of PKU products, as it may lead to “quality use of medications” (QUM) issues. The NPWP

requested that the Drug Utilisation Sub-Committee (DUSC) examine the potential wastage of all PKU products. The object of the examination is to investigate if there has been a marked increase in scripts for the treatment of PKU compared to the expected patient population, which would indicate the possibility of wastage across the indication.

- 5.6 The NPWP supported the listing of PKU Restore[®] as a Restricted Benefit for phenylketonuria on a cost-minimisation basis against Camino Pro Restore[®] at an equivalent price per gram of protein. The NPWP also advised the PBAC to recommend that the DUSC examine the use of all PKU products for any possible QUM issues.

Estimated PBS usage & financial implications

- 5.7 The DPMQ for PKU Restore[®] (\$██████) was derived based on an equivalent cost per gram of PE against the comparator (AEMP = \$██████).
- 5.8 The submission estimated dispensing 53 proposed maximum quantities in the first year, 61 in the second year, and approximately a █% increase applied to subsequent years.
- 5.9 The sponsor estimated a nil financial cost to the PBS, as the product is expected to substitute for Camino Pro Restore[®] and replace it once it is delisted and discontinued.

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

6 PBAC Outcome

- 6.1 The PBAC recommended the listing of PKU Restore[®] for the treatment of phenylketonuria on a cost-minimisation basis against Camino Pro Restore[®] at an equivalent cost per gram of protein.
- 6.2 The PBAC noted the advice of the Nutritional Products Working Party (NPWP) that supported the decision to list PKU Restore[®] on the PBS.
- 6.3 The PBAC accepted Camino Pro Restore[®] as an appropriate comparator for PKU Restore[®].
- 6.4 The PBAC noted that the submission estimated a nil cost to the PBS as it was expected to substitute for a delisted product.
- 6.5 The PBAC agreed with the NPWP's advice to request that the Drug Utilisation Sub-Committee (DUSC) examine the potential wastage of PKU products resulting from an increase in products available with a reasonably short shelf life and high maximum quantities.
- 6.6 In accordance with subsection 101(3BA) of the *National Health Act*, the PBAC advised it is of the opinion that, on the basis of the material available to it at its

November 2016 meeting, PKU Restore® should be treated as interchangeable on an individual patient basis with similar nutritional products.

- 6.7 The PBAC advised that PKU Restore® was suitable for prescribing by nurse practitioners, as nutritional products are currently included for prescribing by nurse practitioners.
- 6.8 The PBAC recommended that the Early Supply Rule should not apply as it has been the PBAC's view that general nutrients be exempt.
- 6.9 The PBAC noted that this submission was not eligible for an Independent Review, as it had received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

7.1 Add new item:

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8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

9 Sponsor's Comment

The sponsor had no comment.