

**5.27 GLYCOMACROPEPTIDE FORMULA WITH AMINO ACIDS
AND LOW PHENYLALANINE,
Sachets containing oral powder 12.5 g, 30 (PKU
GMPPro MIX-IN),
PKU GMPPro MIX-IN[®],
Nutricia Australia Pty Limited**

1 Purpose of Submission

- 1.1 The Category 3 submission requested a General Schedule Restricted Benefit listing of glycomacropeptide formula with amino acids and low phenylalanine, sachets containing oral powder 12.5 g (PKU GMPPro MIX-IN[®]) for the treatment of phenylketonuria (PKU) in children from 3 years of age, and adults.

2 Background

- 2.1 PKU GMPPro MIX-IN had not been considered by the Pharmaceutical Benefits Advisory Committee (PBAC) previously.
- 2.2 Glycomacropeptide formula with amino acids and low phenylalanine is not PBS-listed.
- 2.3 PKU GMPPro MIX-IN 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.

3 Requested listing

- 3.1 The submission requested the following new listing.
Add new medicinal product as follows:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№.of Rpts	Available brands
GLYCOMACROPEPTIDE FORMULA WITH AMINO ACIDS AND LOW PHENYLALANINE					
glycomacropeptide formula with amino acids and low phenylalanine powder for oral liquid, 30 x 12.5 g sachets	NEW	5	5	5	PKU GMPPro MIX-IN
Restriction Summary [new] / Treatment of Concept:					
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					
Administrative Advice: This product does not contain any vitamins, is low in mineral content and is not intended as a sole source of nutrition.					
Indication: Phenylketonuria					
Population criteria: For children from 3 years of age, and adults					

- 3.1 The submission proposed a population criterion, which is inconsistent with the proposed comparators.
- 3.2 The submission noted PKU GMPPro MIX-IN does not contain vitamins, and that it should not be used as a sole source of protein. It must be given in conjunction with natural protein and other nutrients to supply the phenylalanine, fluid and general nutrition requirements of the patient.

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

4 Comparator

- 4.1 The submission nominated PKU Restore® as the main comparator. The submission also nominated tablet-based Phlexy-10®, PKU Easy Tablet® and PKU Easy Microtabs® as additional comparators. The PBAC considered this was appropriate.

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 and welcomed the input from an individual via the Consumer Comments facility on the Pharmaceutical Benefits Scheme (PBS) website. The comments described a range of benefits of treatment with PKU GMPPro MIX-IN including fewer side effects and overall better treatment of a chronic condition such as PKU.

Clinical trials

- 5.3 As a Category 3 submission, no clinical trials were presented in the submission comparing PKU GMPPro MIX-IN to the comparators. The submission stated that PKU GMPPro MIX-IN is nutritionally very similar to PKU Restore, Phlexy-10, PKU Easy Tablet, and PKU Easy Microtabs.
- 5.4 The submission presented a summary of PKU GMPPro MIX-IN patient acceptability Case Studies data to inform gastrointestinal tolerance. The submission stated that PKU GMPPro MIX-IN is very well tolerated with good compliance and acceptability of the dietary regimen.
- 5.5 The submission considered the low-calorie aspect of PKU GMPPro MIX-IN would assist many adult patients who struggle with weight gain and the subsequent increase in the risk of other lifestyle co-morbidities.

Pricing consideration

- 5.6 The submission presented a cost-minimisation analysis of PKU GMPPro MIX-IN compared with the main comparator PKU Restore, based on the same price per gram protein equivalent (PE) of \$0.795 at the approved ex-manufacturer price (AEMP).
- 5.7 As a Category 3 submission, the economic analysis had not been independently evaluated.
- 5.8 The submission proposed an AEMP (\$238.58) equivalent to the main comparator PKU Restore.
- 5.9 The PBAC noted that as PKU GMPPro MIX-IN is a new drug it would be placed on the F1 formulary. Drugs in the F1 formulary are subject to anniversary price reductions with the first reduction being a 5% reduction on the fifth anniversary of listing. The main comparator PKU Restore is listed as the drug glycomacropeptide and essential amino acids with vitamins and minerals and has already been subject to a 5% five-year anniversary price reduction (on 1 April 2019).
- 5.10 The price of PKU GMPPro MIX-IN in comparison to the nominated comparators is presented in the table below. The tablet-based comparators have lower AEMPs however were priced based on per gram PE.

Table 1: Calculated costs versus comparators (PKU GMPPro MIX-IN is a proposed DPMQ)

	PKU GMPPro MIX-IN	PKU Restore	Phlexy-10	PKU Easy Tablet	PKU Easy Microtabs
Presentation	30 x 12.5g 300g PE	60 x 20g sachets 300g PE	75 Tablets 62.25g PE	6 x 77 tablets 70g PE	4 x 110g 77.9g PE
Units	30	60	1 x 75 tablets	6	4
Max quantity of boxes	5 x 30 x 12.5g	5 x 60 x 20g	24 x 75 tablet jars	4 x 6 x 77g	7 x 4 x 110g
g protein equivalent (PE) per serve	10g PE per 12.5g sachet	5g PE per 20g sachet	8.3g PE per 10 tablets	10g PE per 11 tablets	10g PE per 14g tablets
Therapeutic relativity based on PE	1	1	1	1	1
Total PE for maximum quantity	1500g	1500g	1494g	1680g	2200g
AEMP	\$238.58	\$238.58	\$43.86	\$299.47	\$242.91
AEMP per Max Qty	\$1192.90	\$1192.90	\$1052.64	\$1197.88	\$1700.37
AEMP per g PE	\$0.795	\$0.795	\$0.705	\$0.713	\$0.773
DPMQ	\$1316.48	\$1316.48	\$1169.38	\$1321.74	\$1849.27

Source: Table 8 of PKU GMPPro MIX-IN submission main document

AEMP: approved ex-manufacturer price, DPMQ: dispensed price for maximum quantity, g: gram, PE: protein equivalent

Drug cost/patient/year: \$15,797.76

5.11 The above calculation of nutritional product cost per patient per year for the treatment of PKU was derived from the dispensed price for maximum quantity (DPMQ) for one month's supply (\$1,316.48) over 12 months. The submission stated that the quantity of protein substitute/supplement and the dilution should be determined by a clinician or dietitian only, and is dependent on age, bodyweight, and medical condition of the patient. The submission claimed that the protein requirement per day is calculated based on weight (kg) times the correspondent total protein (g/kg/day) and 50-80% of total protein requirements are provided by protein substitute. In this case, each prescription of PKU GMPPro MIX-IN provides 1500 g of protein, which would provide patients who weigh 70 kg a month supply.

Estimated PBS utilisation and financial implications

5.12 The submission used a market share approach to predict the utilisation and estimate the financial implication of PKU GMPPro MIX-IN against the comparators.

5.13 The submission considered 20% of current users of the main comparator PKU Restore may switch to PKU GMPPro MIX-IN in the first 12 months of listing.

5.14 The submission was estimated to cost the PBS \$0 to < \$10 million in Year 6 of listing, with a total net cost to the PBS of \$0 to < \$10 million over the first 6 years of listing. This is summarised in the below table.

Table 2: Estimated use and financial implications for PKU GMPPro MIX-IN

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Number of scripts PKU GMPPro MIX-IN	1 ¹	1 ¹	1 ¹	1 ¹	1 ¹	1 ¹
Cost to PBS/RPBS less copayments	\$2 ²	\$2 ²	\$2 ²	\$2 ²	\$2 ²	\$2 ²
Number of scripts changed listing	1 ¹	1 ¹	1 ¹	1 ¹	1 ¹	1 ¹
Cost to PBS/RPBS less copayments change listing	-\$3 ³	-\$3 ³	-\$3 ³	-\$3 ³	-\$3 ³	-\$3 ³
Net cost to PBS/RPBS	\$2 ²	\$2 ²	\$2 ²	\$2 ²	\$2 ²	\$2 ²

Source: Utilisation and Cost Model Workbook PKU GMPPro MIX-IN

The redacted values correspond to the following ranges:

¹ < 500

² \$0 to < \$10 million

³ net cost saving

- 5.15 As a Category 3 submission, the financial estimates have not been independently evaluated.

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

6 NPWP Consideration

- 6.1 The Nutritional Products Working Party (NPWP) supported the listing of PKU GMPPro MIX-IN for the treatment of phenylketonuria (PKU) in children from 3 years of age, and adults.
- 6.2 The NPWP advised that the comparators PKU Restore, Phlexy-10, PKU Easy Tablet and PKU Easy Microtabs are appropriate.
- 6.3 The NPWP considered the carbohydrate and mineral content are low, and so advised that the AMT description of the product should be changed to 'glycomacropptide formula with amino acids and low phenylalanine'. This has been actioned by the Australian Digital Health Agency at the request of the Secretariat.
- 6.4 The NPWP advised to exclude the proposed population criterion 'For children from 3 years of age, and adults' from the restriction noting this is consistent with the comparators.
- 6.5 The NPWP advised the addition of a cow's milk allergy caution to the restriction is not necessary. The NPWP considered the nutritional label containing the allergy warning would be sufficient.
- 6.6 The NPWP advised that the proposed administration advice should be adjusted to 'This product does not contain any vitamins, is low in mineral content and is not intended as a sole source of nutrition' to be clear on the nutritional content for prescribers and patients.

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 glycomacropeptide formula with amino acids and low phenylalanine (PKU GMPPro MIX-IN[®]) for the treatment of phenylketonuria.
- 7.2 The PBAC noted and agreed with the NPWP advice detailed in Section 6 NPWP consideration.
- 7.3 The PBAC advised that PKU GMPPro MIX-IN is suitable for prescribing by nurse practitioners.
- 7.4 The PBAC recommended that the Early Supply Rule should not apply, as it has been the PBAC's view that general nutrients be exempt.
- 7.5 The PBAC considered the cost-minimisation analysis of PKU GMPPro MIX-IN compared with the main comparator PKU Restore[®] appropriate, based on the same price per gram protein equivalent (PE) of \$0.795.
- 7.6 The PBAC noted the minor cost to Government due to possible switching with the lower AEMP tablet comparators.
- 7.7 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because PKU GMPPro MIX-IN is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over PKU Restore, 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 2009* for Pricing Pathway A were not met.
- 7.8 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 item:

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Restriction Summary [new] / Treatment of Concept:					
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Restriction type: <input checked="" type="checkbox"/> Restricted benefit					
Administrative Advice: This product does not contain any vitamins, is low in mineral content and is not intended as a sole source of nutrition.					
Indication: Phenylketonuria					

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.