

6.19 HIGH FAT FORMULA WITH VITAMINS, MINERALS AND TRACE ELEMENTS AND LOW IN PROTEIN AND CARBOHYDRATE, Oral liquid 250 mL, 30, KetoVie Peptide 4:1, Cortex Health Pty Ltd

1 Purpose of Application

- 1.1 The Category 3 submission requested an amendment to the November 2020 PBAC recommendation for KetoVie Peptide 4:1 to be listed on the basis of cost-minimisation to the newly proposed comparators.

2 Background

Previous PBAC consideration

- 2.1 At the November 2020 PBAC meeting, the PBAC recommended the General Schedule, Restricted Benefit listing of high fat formula with vitamins, minerals and trace elements and low in protein and carbohydrate (KetoVie Peptide 4:1) for ketogenic diet.
- 2.2 The PBAC advised that the inclusion of the cost of preparation time in the cost-minimisation analysis was not appropriate. The PBAC also noted the minor submission provided no clinical evidence that demonstrated superior comparative effectiveness and safety of KetoVie Peptide 4:1 compared with the comparators.
- 2.3 The PBAC considered the requested [REDACTED] % price premium for KetoVie Peptide 4:1 was not well justified and PBAC recommended listing KetoVie Peptide 4:1 with a price based on the same price per kilojoule compared to KetoCal 4:1 (\$0.0042 at the AEMP), but with additional PBS-eligibility criteria.
- 2.4 The PBAC noted the sponsor requested an Authority Required (STREAMLINED) listing. However, the PBAC advised that based on the same price per kilojoule as KetoCal 4:1, a Restricted Benefit listing would be reasonable.
- 2.5 The PBAC considered that the financial estimates were likely to be underestimated as the submission had assumed that all use of KetoVie was in place of KetoCal. However, the listing of KetoVie Peptide 4:1 had the potential to replace both KetoCal and amino acid based preparations and the submission provided no estimate on the number of patients who required tube feeding for ketogenic diet in the private or public hospital system.

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- 2.6 The sponsor indicated in its response to the November 2020 PBAC outcome that they were unable to list KetoVie Peptide 4:1 at the same price per kilojoule as the other formulations due to a significantly high ingredient/manufacturing cost, because of the novel peptide formulation.

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

3 Requested listing

- 3.1 The submission did not request any changes to the listing recommended at the November 2020 PBAC meeting.

- 3.2 Suggested additions are in *italics* and deletions are in strikethrough.

| MEDICINAL PRODUCT medicinal product pack | PBS item code | Max. qty packs | Max. qty units | No.of Rpts | Available brands |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|-------------------|-------------------|---------------|---------------------|
| HIGH FAT FORMULA WITH VITAMINS, MINERALS AND TRACE ELEMENTS AND LOW IN PROTEIN AND CARBOHYDRATE | | | | | |
| high fat formula with vitamins, minerals and trace elements and low in protein and carbohydrate (4:1 ratio medium chain fat to carbohydrate plus protein) liquid, 250 mL, 30 | NEW | 6 | 6 | 5 | KetoVie Peptide 4:1 |
| Restriction Summary [New] | | | | | |
| 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: <i>No increase in the maximum number of repeats may be authorised.</i> | | | | | |
| Indication: Ketogenic diet | | | | | |
| Clinical criteria: | | | | | |
| Patient must have intractable seizures requiring treatment with a ketogenic diet; or | | | | | |
| Patient must have a glucose transport protein defect; or | | | | | |
| Patient must have pyruvate dehydrogenase deficiency | | | | | |
| AND | | | | | |
| Clinical criteria: | | | | | |
| Patient must have severe intestinal malabsorption of whole protein ketogenic diet formula. | | | | | |
| AND | | | | | |
| Clinical criteria | | | | | |
| Patient must have unsuccessfully trialled at least one of the PBS-listed products with the indication of: ‘Ketogenic diet’. | | | | | |
| Prescribing Instructions: | | | | | |
| This product must only be used under strict supervision of a dietitian, together with a metabolic physician and/or neurologist. | | | | | |
| Administrative Advice: Authorities for increased maximum quantities, up to a maximum of 11, may be authorised. <i>Increases in the maximum quantity (packs) of up to twice the value stated may be sought.</i> | | | | | |

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

4 Comparator

- 4.1 The submission presented two modular feeds outlined in Table 1 as comparators, namely Formulation 1 and Formulation 2.

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4.2 The submission compared the proposed daily cost of KetoVie Peptide 4:1 against the daily cost of the comparators.

Table 1: Nutritional composition Formulation 1 and 2 and cost comparison of Formulation 1 and 2 and KetoVie Peptide 4:1.

| Nutritional composition and daily comparator cost | | | | |
|----------------------------------------------------------------------------|------------------------------------------|--------------------------|-----------------------------------|---------------------------------------------------|
| Ingredient (per day) | Cost (DPMQ or to patient) | Pack (bottle/can) | Unit cost (per bottle/can) | PBS cost of constituents per day (at DPMQ) |
| Formulation 1 – (amino acid-based formula prepared from components) | | | | |
| Ross Carb-free formula (Abbott Nutrition), 384 mL | \$14.50 | 384 mL | \$14.50 | |
| Liquigen (Nutricia), 120 mL | \$10.15 | 250 mL | \$21.15 | \$10.15 |
| Essential Amino Acid Mix (Nutricia), 20 g | \$30.73 | 200 g | \$307.30 | |
| Poly-joule (Nutricia), 15 g | \$1.10 | 400 g | \$29.21 | |
| Metamucil, 35 g | \$1.98 | 283 g | \$15.99 | |
| Total for ingredients: | \$58.45 | | | |
| Preparation cost | \$0.00 | | | |
| Total | \$58.45 | | | \$10.15 |
| Formulation 2 (updated, from Nov 2020 submission) | | | | |
| Complete Amino Acid Mix, 40 g | \$28.53 | 200 g | \$142.65 | |
| PolyCal, 3 g | \$0.20 | 400 g | \$27.27 | |
| Benefiber, 13 g | \$0.40 | 730 g | \$22.49 | |
| Betaquik, 115 mL | \$4.68 | 225 mL | \$9.15 | \$4.68 |
| Microlipid, 250 mL | \$40.06 | 89 mL | \$14.26 | |
| Water, 600 mL | \$0.00 | | | |
| NanoVM 9-18 Years, 4 scoops | \$11.33 | 275 g | \$77.89 | |
| Nordic Naturals Ultimate Omega, + ½ tsp | \$1.27 | 237 mL | \$99.95 | |
| Total for ingredients: | \$86.46 | | | |
| Preparation cost | \$0.00 | | | |
| Total | \$86.46 | | | \$4.68 |
| Comparator and KetoVie Peptide 4:1 energy equivalent costs | | | | |
| Cost comparison | Daily cost (DPMQ for PBS, or OTC) | | | |
| | Vs formula 1 | Vs. formula 2 | Vs weighted formula** | |
| KetoVie 4:1 Peptide (1250 mL daily)* | \$ [REDACTED] | - | \$ [REDACTED] | |
| KetoVie 4:1 Peptide (1000 mL daily)* | - | \$ [REDACTED] | | |
| PBS cost-offsets with amino acid-based formula | \$10.15 | \$0.58 | \$8.78 | |
| Non-PBS cost-offsets with amino acid-based formula | \$48.30 | \$81.79 | \$56.67 | |
| Extra cost with use of KetoVie Peptide (per day) | \$ [REDACTED] | -\$ [REDACTED] | \$ [REDACTED] | |

Source: Table 1.5 of the submission, p8 of the submission & Table 3.2, p16 of the submission.

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* Proposed AEMP is \$ [REDACTED] for 250 mL x 30 cartons. This equates to a DPMQ of \$ [REDACTED] for the PBS Maximum quantity of 6. Formula 1 provides the same energy per day as 1,280 mL of KetoVie Peptide 4:1 (with assumed use 1,250 mL for practical use of 250 mL cartons), Formula 2 provides the same energy as 1000 mL per day of KetoVie Peptide 4:1.

** weighted used is 75% for Formula 1 and 25% for formula 2

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 that this item received no consumer comments.

Clinical claim

5.3 The submission claimed non-inferior comparative effectiveness and safety of KetoVie Peptide 4:1 compared with Formulation 1 and Formulation 2.

Product cost/patient/year: \$ [REDACTED]

5.4 The estimated product cost/patient/year would be \$ [REDACTED] based on 12 prescriptions per year at the AEMP of \$ [REDACTED]. The actual cost will vary due to variations in individual patient needs.

Estimated PBS utilisation and financial implications

5.5 The submission no longer presented KetoCal (\$0.0042 per kJ of energy) as a comparator. However, it proposed KetoVie Peptide 4:1 at a price of \$ [REDACTED] per kJ of energy that is still 100% more than the price based on PBAC's recommendation of cost-minimisation to KetoCal. The proposed price is also significantly higher than the other peptide-based formulas on the PBS, e.g. Nutrini Peptisorb (\$0.0047 per kJ) and Nestle Peptamen Junior (\$0.0047 per kJ).

5.6 The submission stated that the estimated use and financial implications were the same as the November 2020 submission.

5.7 The submission estimated a net cost to the PBS of \$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 Table 2.

5.8 The submission considered KetoVie Peptide 4:1 would not replace KetoCal product but KetoVie Peptide 4:1 would be expected to replace use of the non-PBS amino acid-based formulations. The financial estimates in this submission do not reflect this consideration.

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Table 2: Estimated use and financial implications

| | Year 1 | Year 2 | Year 3 | Year 4 | Year 5 | Year 6 |
|---------------------------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Estimated extent of use | | | | | | |
| Number of scripts dispensed ^a | ■ ¹ | ■ ¹ | ■ ¹ | ■ ¹ | ■ ¹ | ■ ¹ |
| Nutritional product costs | | | | | | |
| Cost of nutritional product to PBS | \$■ ² | \$■ ² | \$■ ² | \$■ ² | \$■ ² | \$■ ² |
| Less patient co-payments | -\$■ ² | -\$■ ² | -\$■ ² | -\$■ ² | -\$■ ² | -\$■ ² |
| Estimated net financial implications | | | | | | |
| Net cost to PBS | \$■ ² | \$■ ² | \$■ ² | \$■ ² | \$■ ² | \$■ ² |

^a Based on past and projected future use of KetoCal, usage of KetoVie Peptide 4:1 has been estimated. It is assumed that all use of KetoVie is adjunctive, i.e. no reduced use of any existing PBS products.

Source: Table 4.7 & Table 4.8 of the submission, p22 of the submission.

The redacted values correspond to the following ranges:

¹ < 500

² \$0 to < \$10 million

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

6 NPWP Consideration

- 6.1 The Nutritional Products Working Party (NPWP) maintained its support for listing KetoVie Peptide 4:1 to address clinical need for a small number of patients. However, the NPWP advised that the revised comparators may not be applicable to the requested population, such that the cost-minimisation calculation and proposed price were not supported. The NPWP suggested that the sponsor provide a revised cost-minimisation calculation using the Australian products and peptide-based formula as outlined.
- 6.2 With respect to the clinical need of KetoVie Peptide 4:1, the NPWP considered that:
- The product would provide a clinical benefit to a small cohort of patients because there is nothing similar on the PBS for children with epileptic conditions who experience gastrointestinal tract intolerance to other products or those who are intolerant to both cow's milk and soy milk protein.
 - The estimated number of scripts is likely an underestimate of the true uptake.
 - The product would provide significant convenience and reduction in risk of contamination compared to the burden from the complex regimen and hygiene considerations required to make up a modular feed from a number of ingredients.
- 6.3 With respect to the appropriateness of the comparators, the NPWP considered that:
- In practice, most patients with gastrointestinal tract intolerance would currently be using modular feed, which can be composed in a variety of ways and tends to vary by hospital.

- KetoVie Peptide 4:1 would most likely replace modular feed but may also replace peptide-based formula.
 - The newly proposed comparators (Formulation 1 and Formulation 2) are inappropriate.
 - Formulation 1 is soy-based (intact protein) rather than peptide-based and may not be suitable for all targeted patients.
 - Formulation 2 contains American products that are not readily available in Australia.
 - Formulation 2 could be an appropriate comparator if it was modified with Australian ingredients such that:
 - Carb Plus or Polyjoule be used instead of Polycal
 - Calogen be used instead of Microlipid
 - FruityVits be used instead of NanoVM.
 - Peptide-based formula (not ketogenic but containing medium chain triglyceride), such as Nutrini Peptisorb and Nestle Peptamen Junior, may be appropriate comparators.
 - A revised cost-minimisation calculation from the sponsor with calculation of Australian ingredients used in Formulation 2 and relevant peptide-based formula would be useful to inform further consideration of the proposed price.
- 6.4 With respect to the revised cost-minimisation calculation, the NPWP considered that the method used to determine the price of KetoVie Peptide 4:1 was not appropriate because the newly proposed comparators were not appropriate.
- 6.5 With respect to the restrictions, the NPWP considered that STREAMLINED or Authority Required (telephone/electronic) restriction would be appropriate to minimise use outside the restriction if KetoVie Peptide 4:1 was recommended at the proposed price, for example, in patients without intolerance to intact protein.

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

7 PBAC Outcome

- 7.1 The PBAC recommended the Authority Required (telephone/electronic) listing of high fat formula with vitamins, minerals and trace elements and low in protein and carbohydrate (KetoVie Peptide 4:1) for ketogenic diet. The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of KetoVie would be acceptable if it were cost-minimised against KetoCal 4:1 with approximately █% premium over KetoCal 4:1.
- 7.2 The PBAC noted and agreed with the advice of the NPWP.
- 7.3 The PBAC recalled its November 2020 recommendation for KetoVie Peptide 4:1 at the same price per kilojoule as KetoCal 4:1 (\$0.0042 per kJ). The PBAC did not accept the

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applicant's request for a price of \$ [REDACTED] per kJ, as the submission did not demonstrate superior efficacy and safety compared with comparators, nor the cost offset claimed for preparation time.

- 7.4 The PBAC noted that this resubmission presented a revised cost minimisation calculation to support the requested price (\$ [REDACTED] per kJ) based on two new proposed comparators (Formulation 1 and Formulation 2). The PBAC agreed with the NPWP that the new proposed comparators were not appropriate.
- 7.5 The PBAC noted the submission claimed non-inferior efficacy over the newly proposed comparators and considered that KetoVie Peptide 4:1 provides:
- significant convenience and reduction in risk of contamination compared to the burden from the complex regimen and hygiene considerations required to make up a modular feed from a number of ingredients
 - a clinical benefit to a small cohort of patients because there was nothing similar on the PBS for children with epileptic conditions who experienced gastrointestinal tract intolerance to other products or those who were intolerant to both cow's milk and soy milk protein.
- 7.6 The PBAC noted that the pre-PBAC response provided a revised calculation with Australian ingredients in Formulation 2 in response to the NPWP advice. The PBAC considered the revised calculation did not justify the requested price for KetoVie Peptide 4:1, which was significantly higher than the other PBS-listed peptide-based formulas such as Nutrini Peptisorb (\$0.0047 per kJ) and Nestle Peptamen Junior (\$0.0047 per kJ).
- 7.7 The PBAC noted that the financial estimates were unchanged from the November 2020 submission. The PBAC reaffirmed its advice that the financial estimates were likely to be underestimated. The submission assumed all use of KetoVie was in place of KetoCal. However, the listing of KetoVie Peptide 4:1 may replace both KetoCal and amino acid based preparations. Additionally, the submission provided no estimate of the number of patients who required tube feeding for ketogenic diet in the private or public hospital system.
- 7.8 The PBAC recognised a small additional clinical benefit of KetoVie Peptide 4:1 over KetoCal 4:1 for a small cohort of patients with epileptic conditions who experienced gastrointestinal tract intolerance to other products or those who were intolerant to both cow's milk and soy milk protein. The PBAC recommended KetoVie Peptide 4:1 at a price no more than \$ [REDACTED] per kJ (approximately [REDACTED]% premium over KetoCal 4:1). At this price, the PBAC estimated a net cost to the PBS of \$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.
- 7.9 The PBAC recalled the sponsor requested an Authority Required (STREAMLINED) listing. The PBAC considered an Authority Required (telephone/online PBS

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Authorities system) restriction would be appropriate to minimise use outside the recommended population, such as in patients without intolerance to intact protein.

- 7.10 The PBAC advised that KetoVie products are suitable for prescribing by nurse practitioners.
- 7.11 The PBAC recommended that the Early Supply Rule should not apply.
- 7.12 The PBAC considered it appropriate that administrative advice be included in the restriction to enable approval for an increase in the maximum quantity (packs) of up to twice the value through Services Australia.
- 7.13 The PBAC advised that, because KetoVie products are not expected address a high and urgent unmet clinical need given the presence of alternative therapies, the criteria prescribed by the National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009 for Pricing Pathway A were not met.
- 7.14 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 medicinal product packs as follows:

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| MEDICINAL PRODUCT medicinal product pack | PBS item code | Max. qty packs | Max. qty units | No. of Rpts | Available brands |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|-------------------|-------------------|----------------|---------------------|
| HIGH FAT FORMULA WITH VITAMINS, MINERALS AND TRACE ELEMENTS AND LOW IN PROTEIN AND CARBOHYDRATE | | | | | |
| high fat formula with vitamins, minerals and trace elements and low in protein and carbohydrate (4:1 ratio medium chain fat to carbohydrate plus protein) liquid, 250 mL, 30 | NEW | 6 | 6 | 5 | KetoVie Peptide 4:1 |
| Restriction Summary [New] | | | | | |
| 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"/> Authority Required - (telephone/online PBS Authorities system) | | | | | |
| Administrative Advice: No increase in the maximum number of repeats may be authorised. | | | | | |
| Indication: Ketogenic diet | | | | | |
| Clinical criteria: | | | | | |
| Patient must have intractable seizures requiring treatment with a ketogenic diet; or | | | | | |
| Patient must have a glucose transport protein defect; or | | | | | |
| Patient must have pyruvate dehydrogenase deficiency | | | | | |
| AND | | | | | |
| Clinical criteria: | | | | | |
| Patient must have severe intestinal malabsorption of whole protein ketogenic diet formula. | | | | | |
| AND | | | | | |
| Clinical criteria | | | | | |
| Patient must have unsuccessfully trialed at least one of the PBS-listed products with the indication of: 'Ketogenic diet'. | | | | | |
| Prescribing Instructions: | | | | | |
| This product must only be used under strict supervision of a dietitian, together with a metabolic physician and/or neurologist. | | | | | |
| Administrative Advice: Increases in the maximum quantity (packs) of up to twice the value stated may be sought. | | | | | |

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.