

## 5.18 CARBOHYDRATE FORMULA WITH MINERALS

Oral liquid: powder for, 21g, 31g, 42g, 52g sachets, 30 SOS10<sup>®</sup>, SOS15<sup>®</sup>, SOS20<sup>®</sup>, SOS25<sup>®</sup>,  
Vitaflo Australia Pty Ltd.

### 1 Purpose of Application

- 1.1 The minor submission requested a Restricted Benefit listing for proven inborn errors of protein metabolism and proven inborn errors of fat metabolism.

### 2 Requested Listing:

- 2.1 The submission requested the following new listing:
- 2.2 Suggestions and additions proposed by the Secretariat to the requested listing were added in italics and suggested deletions were crossed out with strikethrough.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer
CARBOHYDRATE FORMULA WITH MINERALS			Vitaflo Australia Pty Ltd
Oral liquid, powder for:			
30 × 21g sachets	4	5	SOS 10
30 × 31g sachets	4	5	SOS 15
30 × 42g sachets	4	5	SOS 20
30 × 52g sachets	4	5	SOS 25

<b>Category / Program</b>	GENERAL – General Schedule (Code GE)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Condition:</b>	Proven inborn errors of protein metabolism Proven inborn errors of fat metabolism
<b>PBS Indication:</b>	Proven inborn errors of protein metabolism Proven inborn errors of fat metabolism
<b>Restriction Level / Method:</b>	<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
<b>Clinical criteria:</b>	Patient must be unable to meet their energy requirements with permitted food and formulae.
<b>Cautions</b>	<del>Not for parenteral use</del>

- 2.3 The Secretariat notes that the sponsor's proposed drug name (glucose polymer) is not currently a valid Legal Instrument name. The Secretariat has amended the drug name to "Carbohydrate formula with Minerals" to align with the Australian medicines terminology (AMT) description provided by the Australian Digital Health Agency.
- 2.4 The sponsor's proposed drug name, glucose polymer, is not currently listed as a standalone listed drug in the National Health (Listing of Pharmaceutical Benefits) Instrument 2012 (PB 71 of 2012) (the Legal Instrument). Similar products on the PBS, such as ProZero<sup>®</sup>, Sno-Pro<sup>®</sup> and Duocal<sup>®</sup> contain triglycerides (fats), which are included in the Legal Instrument name. Duocal<sup>®</sup>'s Legal Instrument name is "Triglycerides, medium chain and long chain with glucose polymer" while ProZero<sup>®</sup> and Sno-Pro<sup>®</sup> are listed under "Triglycerides, long chain with glucose polymer". The Secretariat proposes to list the sponsor's nutritional product under the Legal Instrument name of "Carbohydrate formula with Minerals", if the submission receives a positive recommendation.
- 2.5 The sponsor proposed an additional indication of "proven inborn errors of fat metabolism". There are currently no products on the PBS listed for this indication. The Nutritional Products Working Party (NPWP) and the PBAC were asked to comment on the suitability of the products for the proposed indication.

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

### **3 Background**

- 3.1 The sponsor 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 submission has not been considered by PBAC previously.
- 3.3 The submission included four different strengths of carbohydrate solution; SOS 10<sup>®</sup> provides a 10% carbohydrate solution, SOS 20<sup>®</sup> a 20% solution, and so on. The sponsor claimed that the range of solutions caters to different age groups, from infants to patients aged over 10 years.
- 3.4 The SOS<sup>®</sup> products contain no protein, therefore no nitrogen, and no fats. Similar PBS-listed products such as Prozero<sup>®</sup> and Duocal<sup>®</sup> do contain fats; 3.8g fat per 100mL and 5.6g fat per 100mL respectively. Because of the products' lack of fats, the sponsor has proposed an additional indication for patients with inborn errors of metabolism (IEM) of fat. No clinical data were provided to support the inclusion of a new indication to the PBS.
- 3.5 The sponsor's products would be unique in nutritional composition on the PBS if listed and as such the sponsor proposed the drug name "glucose polymer". The currently PBS-listed products similar to SOS<sup>®</sup> are long or medium chain triglycerides with glucose polymer; therefore, if listed, the SOS<sup>®</sup> products will be unique in

containing glucose polymer alone. The Australian Digital Health Agency has proposed an AMT name of “carbohydrate formula with minerals”.

*For more detail on PBAC’s view, see section 6 “PBAC outcome”*

#### **4 Comparator**

- 4.1 The submission nominated ProZero® as the main comparator. ProZero® is an oral liquid for proven IEM of protein, and does not contain protein and micronutrients.
- 4.2 The key differences between the main comparator and SOS® products are the presentation, additional strengths, and nutritional composition. ProZero® is a pre-made oral liquid solution available in 250mL cans or 1L bottles, and contains long chain triglycerides with dried glucose syrup. The SOS® products are four different doses of powder sachets, ranging from 21g to 52g, to be reconstituted into a 200mL solution. The SOS® products also contain dried glucose syrup, but do not contain long or medium chain triglycerides.
- 4.3 The additional doses may also provide added convenience of use for different patients, as calculating the necessary carbohydrate content is not needed.
- 4.4 The sponsor proposed that the products can replace, or be used in combination with, other glucose polymer products for proven IEM of protein.

#### **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
<b>Direct randomised trial</b>		
-	Gokem-Ozel, H., Daly, A., Davies, P., Chahal, S., MacDonald, A., Errors in emergency feeds in inherited metabolic disorders: a randomised controlled trial of three preparation methods	Archives of Disease in Childhood. 2010; 95: 776-780

Source: SOS clinical trial paper. Compiled during the minor overview

- 5.4 The trial aimed to find which method of preparing a glucose polymer-based emergency feed (EF) lead to decreased errors made by carers of patients with IEM. The tested methods were SOS<sup>®</sup> pre-measured sachets, measuring powder using scoops, or weighing powder using digital scales. The overall conclusion was that all preparation methods were likely to be more carbohydrate-concentrated than the target concentration, mostly due to the carers under-measuring the amount of water. The researchers stated that over-concentration of EFs is a common carer error. Over-concentration of carbohydrates can lead to diarrhoea and potentially the exacerbation of the patient's existing metabolic disorder. Weighing using digital scales had the highest likelihood of preparation errors. The pre-measured sachets had no notable differences in accuracy compared to scoops. It was concluded that the pre-measured sachets were most likely to create an EF concentration within 20% accuracy.
- 5.5 In consideration of the submission, the Nutritional Products Working Party (NPWP) noted that:
- The proposed listing and restriction criteria were not appropriate, as the requested indications may be broadly interpreted and administered by clinicians. The NPWP raised concerns over the risk of use outside of the restrictions.
  - The comparator, ProZero<sup>®</sup>, was considered inappropriate as it contains fats while the product does not. Instead, the NPWP noted that Poly-Joule<sup>®</sup> and Carb Plus<sup>®</sup> were more suitable, due to their wide use in patients with conditions related to the sponsor's proposed indications. While not listed on the PBS, Poly-Joule<sup>®</sup> and Carb Plus<sup>®</sup> are available over the counter (OTC) at a significantly lower price than the proposed comparator, and are of a similar composition to the SOS<sup>®</sup> formulas.
  - Based on the NPWP's clinical experience, the sponsor had underestimated the number of patients expected to use the treatment per year. The NPWP estimated the usage to be much higher, which could lead to a higher cost to the Government than the sponsor predicted.
  - A potentially high risk of wastage could occur under the proposed maximum quantity (MQ) requested by the sponsor. The sponsor assumed patients would use 4 cartons of 30 sachets per month, but the NPWP noted that patients are likely to use the product sporadically due to combining different brands of carbohydrate formulae. There is also an added risk of the short shelf life of the sponsor's product, as well as similar products. The NPWP also raised concerns that the product is likely to expire before the patient consumes the entire proposed MQ.
- 5.6 The NPWP did not support the listing of the SOS<sup>®</sup> products on the basis of an inappropriate comparator, lack of clarity around the proposed indication, high risk of use outside the restriction, and the risk of wastage.

***Estimated PBS usage & financial implications***

- 5.7 The DPMQ for the SOS<sup>®</sup> products (\$██████ for SOS 10<sup>®</sup>, \$██████ for SOS 15<sup>®</sup>, \$██████ for SOS 20<sup>®</sup>, and \$██████ for SOS 25<sup>®</sup>) were derived based on an equivalent cost per kilojoule of energy compared with the comparator (\$0.0039).

- 5.8 The comparator received a statutory F1 5% price decrease, effective 1 April 2016. The sponsor has submitted a request to reverse the price decrease for the comparator, and other affected brands, for consideration at the November PBAC meeting (item 8.02). The sponsor has therefore calculated the comparator's cost per kJ based on the AEMP from 1 March 2016; a date prior to the price decrease.

The price per kJ for the comparator under the current AEMP (i.e. post 1 April 2016) was not provided by the sponsor.

The Secretariat calculated the price per kJ from the current AEMP for ProZero® 1 L at ( $\$61.76 \div 2,780 \text{ kJ} = \$0.0037/\text{kJ}$ ).

This would have an effect on the DPMQ for all the SOS® formulations.

- 5.9 The sponsor claimed that the additional indication for proven IEM of fat will result in a minimal financial cost to the PBS, as the patient population is low.
- 5.10 The cost to the PBS is uncertain, as the proposed additional indication does not currently have any related products listed on the PBS. No new clinical data were included in the submission to support the additional indication of proven inborn errors of fat metabolism.

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

## **6 PBAC Outcome**

- 6.1 The PBAC did not recommend the listing of carbohydrate formula with minerals for the treatment of proven inborn errors of protein metabolism and proven inborn errors of fat metabolism. The decision was based on the potential of product wastage and a lack of clarity surrounding the indications. The PBAC considered there was a high risk of use outside the restriction, based on the current wording.
- 6.2 The PBAC noted the advice of the Nutritional Products Working Party (NPWP) that supported the decision to not recommend listing the SOS® products on the PBS.
- 6.3 The PBAC did not accept ProZero® as an appropriate comparator to the SOS® products due to the differences in composition. The PBAC agreed with the NPWP's suggested comparators as stated in 5.3.
- 6.4 The PBAC agreed with the NPWP's advice that a potentially high risk of wastage could occur under the proposed maximum quantity (MQ) of 30 sachets, requested by the sponsor. The PBAC noted that patients are likely to use the product sporadically, and may not consume the total proposed MQ before the product expires.
- 6.5 The PBAC requested that the sponsor provide patient data on the new proposed indication for "proven inborn errors of fat metabolism" for any potential minor re-submission in the future.

- 6.6 The PBAC agreed with the NPWP's concern over the use of SOS® products outside of the proposed restrictions, as the indications "proven inborn errors of protein metabolism" and "proven inborn errors of fat metabolism" can be broadly interpreted by clinicians.
- 6.7 The PBAC noted that this submission is eligible for an Independent Review.

**Outcome:**

Rejected

**7 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.

**8 Sponsor's Comment**

The sponsor had no comment.