6.16 TRIGLYCERIDES, LONG CHAIN WITH GLUCOSE POLYMER, Oral liquid 1 L, 6 (ProZero), ProZero®, VITAFLO AUSTRALIA PTY LIMITED

1 Purpose of Submission

1.1 The Category 3 submission requested an amendment to the restriction level of PBS-listed triglycerides, long chain with glucose polymer 6 x 1 L cartons (ProZero®) (hereafter referred to as ProZero 1 L) for the treatment of proven inborn errors of protein metabolism from Restricted Benefit to Authority Required (STREAMLINED).

1.2 The submission also requested an amendment to the existing clinical criteria of ProZero 1 L and the inclusion of new population criteria (children aged 1 year or older, pre-conception/pregnant women, elderly ≥65 years).

2 Background

2.1 ProZero 1 L is currently listed on the PBS as a General Schedule Restricted Benefit listing for proven inborn errors of metabolism (IEpM) for patients who are unable to meet their energy requirements with permitted food and formulae.

Registration status

2.2 The submission confirmed that ProZero 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.

2.3 As ProZero 1 L is marketed as a nutritional product and not a therapeutic good, it is not registered in the Australian Register of Therapeutic Goods.

Previous PBAC consideration

2.4 At its November 2009 meeting, the PBAC recommended ProZero 1 L for patients with proven inborn errors of protein metabolism at the same price per gram of protein (ex-manufacturer) as Duocal® (November 2009 PBAC Outcomes – Positive Recommendations). ProZero 1 L was listed on the PBS on 1 March 2010.

2.5 At its March 2018 meeting, the PBAC noted the change to the formulation of ProZero products (not affecting the nutritional properties) for proven inborn errors of metabolism and that the change would not alter the listing of ProZero on the PBS (Paragraph 6.1, Triglycerides long chain (ProZero) Public Summary Document [PSD], March 2018).

2.6 At its March 2024 meeting, the PBAC considered a request to delist ProZero 1 L and ProZero 250 mL from the PBS. The submission stated that the request to delist both forms of ProZero was due to financial unviability. The PBAC advised that delisting may result in an unmet clinical need and the Department sought to retain this product in line with this advice. Following consultation with key opinion leaders of IEpM, the sponsor wished to only proceed with the delisting of the 250 mL form of ProZero. ProZero 250 mL was delisted from the PBS on 1 September 2024.

3 Requested listing

3.1 The submission requested the following changes to the existing listing of ProZero 1 L. Suggested additions are in italics and deletions are in strikethrough.

MEDICINAL PRODUCT medicinal product pack		**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
TRIGLYCERIDES LONG CHAIN WITH GLUCOSE POLYMER						
triglycerides long chain with glucose polymer oral liquid, 6 x 1 L cartons		9309Y	4	4	5	ProZero
Restriction Summary [new] / Treatment of Concept: [new]						
	Category / Program: ☒ GENERAL - General Schedule (Code GE)					
	Prescriber type: ☒Medical Practitioners ☒Nurse practitioners					
	Restriction type: ☒~~Restricted benefit~~ ☒Authority Required (Streamlined) [new/existing code]					
	Indication: Proven inborn errors of protein metabolism					
	Clinical criteria:					
	Patient must be unable to meet their energy requirements with permitted food and formulae					
	AND					
	~~**Treatment criteria**~~ ***Clinical criteria:***					
	Patient must require treatment with a very low protein, increased caloric diet.					
	AND					
	~~**Treatment criteria**~~ ***Clinical criteria:***					
	The treatment must be for the purpose of maintaining metabolic control and appropriate growth for at least 6 months: *or*					
	The treatment must be for the purpose of achieving metabolic control for at least 3 months: *or*					
	The treatment must be for the purpose of maintaining metabolic control and preventing metabolic decompensation for at least 6 months					
	Population criteria:					
	Patient must be ~~*a child*~~ aged 1 year or older: *or*					
	Patient must be aged *65 years or older, or*					
	Patient must be one of: (i) planning conception, (ii) pregnant.					

4 Consideration of the evidence

Sponsor hearing

4.1 There was no hearing for this item.

Consumer comments

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

Justification for request

4.3 The submission stated that the proposed amendment will ensure continued access to vulnerable patients who require the product as an essential component of their dietary therapy.

4.4 The submission nominated Sno-Pro® (triglycerides long chain with glucose polymer oral liquid, 27 x 200 mL cartons) as the main comparator and stated that ProZero is also therapeutically equivalent to Duocal (triglycerides medium chain and long chain with glucose polymer powder for oral liquid, 400 g). Both Sno-Pro and Duocal are on the PBS as General Schedule Restricted Benefit listings for IEpM (10189G and 3136C respectively).

4.5 The submission stated that, of the therapeutically equivalent products on the PBS, ProZero is the only product that does not contain medium chain triglycerides.

Economic analysis

4.6 The submission requested no changes to the pricing arrangement for the current listing of ProZero 1 L (approved ex-manufacturer price (AEMP) of $55.58).

4.7 The submission indicated that the sponsor intends to submit a separate application requesting [redacted]. This is not part of the current submission.

Drug cost/patient/year: $3,107.64

4.8 The submission estimated the net cost/patient per year to be $3,107.64, based on 12 scripts per year ($258.97 x 12), noting that the actual cost may vary due to variations in individual patient needs.

Estimated PBS usage and financial implications

4.9 The submission estimated a 40% decrease in the prescription of ProZero 1 L following the proposed changes in its PBS listing. The evaluation examined the estimated change in utilisation by introducing the new population criteria (Table 1). Data was provided for the supply of PBS items 9309Y and 9308X by patient sex and age. The following patient groups were included to estimate the size of the new market:

- Female and male patients aged 1 to 15 years. The ABS Census definition was used to define a child as being aged 15 years or under. As per the proposed restriction, patients under one year of age were excluded;

- Females aged 16 to 44 years. Based on the ABS definition of childbearing age[1] to reflect patients planning conception or who are pregnant; and
- Male and female patients who were 65 years or older.

Male patients aged 16 to 64 years were excluded. The evaluation noted that the decrease in the PBS utilisation of ProZero listings (ProZero 1 L and 250 mL) following the proposed changes was overestimated by the submission (Table 1). The 250 mL form was included in the estimates as the 1 L market has likely assumed the 250 mL market since it was delisted from the PBS on 1 September 2024.

Table 1: PBS utilisation of ProZero listings (items 09309Y and 09308X) from 1 July 2023 to 30 June 2024

	Patients	Prescriptions supplied	Benefits paid
Current market	243	909	$239,040
*Restricted market - children aged from 1-15 years, females aged 16-44 years (pre-conception/pregnant women), female and male patients aged 65 years or older	188	655	$173,910
Difference	**-23%**	**-28%**	**-27%**

Source: Table provided by the evaluation

*Men aged 16 to 64 years, Women aged 45 to 64 years and Children under 1 year were excluded from the restricted market.

Data was extracted from the PBS database maintained by Department of Health and Aged Care, processed by Services Australia based on the date of supply.

4.10 The evaluation further showed that since its listing in 2010, the PBS utilisation for ProZero (1 L and 250 mL) has been unstable, reaching a high of 1,061 prescriptions in 2016 (Table 2).

Table 2: Utilisation of PBS items '09309Y' (ProZero 1 L) and'09308X' (ProZero 250 ml) by year

Year	Patients	Prescriptions supplied	Benefits paid
2010	209	409	$131,000
2011	264	715	$225,281
2012	284	845	$249,705
2013	316	1,012	$303,900
2014	304	987	$303,095
2015	282	1,021	$302,906
2016	270	1,061	$299,770
2017	252	990	$282,923
2018	251	1,054	$306,683
2019	245	1,043	$299,862
2020	252	1,051	$280,480
2021	257	998	$262,232
2022	263	970	$254,773
2023	259	938	$246,240
2024 (YTD 30 June)	193	418	$110,561

Source: Table provided by the evaluation

Data was extracted from the PBS database maintained by Department of Health and Aged Care, processed by Services Australia based on the date of supply.

[1] https://www.abs.gov.au/articles/women-childbearing-age

4.11 The submission assumed no growth for the proposed market across the forward estimates. *This is not appropriate. The growth rate should be revised using trend line projection from the historical data.*

4.12 Table 3 presents the estimated extent of use, cost of proposed changes and the net financial implications to the PBS/RPBS. The financial impact to Services Australia will be determined by that agency as part of the post PBAC process.

4.13 The submission included the cost savings from the delisting of ProZero 250 mL into the financial estimates for the restriction amendments for ProZero 1 L. The evaluation noted that it is inappropriate to include the offset cost of the ProZero 250 mL delist to the proposed listing. The patients previously being prescribed ProZero 250 mL are instead likely to be incorporated into the 1 L market and as such, the estimated population for ProZero 1 L is likely further underestimated.

4.14 The submission estimated that the total number of < 500 patients (< 500 patients per year) will receive 500 to < 5,000 scripts (< 500 scripts per year) over the first six years of listing.

4.15 The submission estimated that the proposed changes to ProZero 1 L listing will result in a net cost saving to the PBS/RPBS over a period of six years. This is likely to be an overestimate based on the analysis from the evaluation above.

Table 3: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of scripts	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Estimated financial implications to PBS						
New listing	$[redacted][2]	$[redacted][2]	$[redacted][2]	$[redacted][2]	$[redacted][2]	$[redacted][2]
Changed listing	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]
Net cost to PBS	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]	-$[redacted][3]
Net financial implications						
Net cost to PBS/RPBS	**-$[redacted][3]**	**-$[redacted][3]**	**-$[redacted][3]**	**-$[redacted][3]**	**-$[redacted][3]**	**-$[redacted][3]**

Source: *Submission's financial model spreadsheet (20 August 2024).
Abbreviations: PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme.
*The submission used outdated copayments of $41.30 and $6.60 in the financial estimates. The evaluation amended the co-payments to reflect the 2024 figures of $31.60 and $7.70.
The redacted values correspond to the following ranges:
[1] *< 500*
[2] *$0 to < $10 million*
[3] *net cost saving*

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

5 NPWP consideration

5.1 The NPWP did not support the request to increase the authority level for ProZero 1 L from Restricted Benefit to Authority Required (STREAMLINED), nor did it support the inclusion of the proposed new population criteria (children aged 1 year or older, pre-conception/pregnant women, elderly ≥ 65 years).

5.2 The NPWP recalled that it had provided advice regarding the sponsor requested delisting of this product. The sponsor had previously indicated that ProZero (250 mL and 1 L) was no longer financially viable to be listed on the PBS due to increased costs of global shipping and consumer price index. The NPWP had identified the importance of having a range of products available and raised concern that there will be an unmet clinical need for certain patients (e.g., 6–12-month-old infants, teenagers and young adults) if ProZero was to delist. The NPWP recalled that only ProZero 250 mL was delisted from the PBS on 1 September 2024.

5.3 The NPWP considered that the revised target population, particularly by age, could not be clinically justified and advised that these proposed changes may result in an unmet clinical need for some patients who are currently receiving PBS-subsidised access to ProZero 1 L.

5.4 The NPWP suggested that a reduction in the maximum quantity may be a more appropriate mechanism for ensuring continued supply and access, rather than restricting the eligible population. Patients currently receive 24 L per dispensing. The NPWP advised that most patients would be using 250-500 mL per day, thus 15 L would be at least a month's supply for most patients. The NPWP noted that each 1 L carton needs to be used within 48 hours of opening, which is also consistent with 15 L supply per month.

5.5 The NPWP agreed with the evaluation that a 40% decrease in the prescriptions of ProZero 1 L following the proposed changes in its PBS listing is likely an overestimate.

5.6 The NPWP advised that the overall financial impact due to the requested amendments is uncertain and agreed with the evaluation that it is inappropriate to include the offset cost of the ProZero 250 mL delist.

6 PBAC Outcome

6.1 The PBAC recommended reducing the maximum quantity packs of triglycerides, long chain with glucose polymer 6 x 1 L cartons (ProZero®) for the treatment of proven inborn errors of protein metabolism from 4 (24 L) to 3 (18 L). The PBAC did not recommend the request to increase the authority level of ProZero 1 L for the treatment of proven inborn errors of protein metabolism from Restricted Benefit to Authority Required (STREAMLINED), nor did it recommend the inclusion of new population criteria (children aged 1 year or older, pre-conception/pregnant women, elderly ≥ 65 years) for the existing ProZero 1 L listing.

6.2 The PBAC noted previous advice from the NPWP that there would be an unmet clinical need for certain patients (e.g., 6–12-month-old infants, teenagers and young adults) if ProZero was to delist. The PBAC also noted that only ProZero 250 mL was delisted from the PBS on 1 September 2024.

6.3 The PBAC noted and supported the NPWP's advice that the revised target population, particularly by age, could not be clinically justified and advised that these proposed

changes may result in an unmet clinical need for some patients who are currently receiving PBS-subsidised access to ProZero 1 L.

6.4 The PBAC agreed with the NPWP that a reduction in the maximum quantity may be a more appropriate mechanism for ensuring continued supply and access, rather than restricting the eligible population. The PBAC noted that patients currently receive 24 L per dispensing (6 x 1 L cartons, maximum quantity of 4). Noting that the quantity is delivered in multiples of 6 cartons, the PBAC recommended reducing the maximum quantity packs from 4 (24 L) to 3 (18 L), consistent with the usual 250-500 mL per day dosage.

6.5 The PBAC noted that the submission included the cost savings from the delisting of ProZero 250 mL into the financial estimates for the restriction amendments for ProZero 1 L. The PBAC agreed with the evaluation that this was inappropriate.

6.6 The PBAC noted this submission is not eligible for an Independent Review because it received a positive recommendation.

Outcome:
Recommended

7 Recommended listing

7.1 Amend maximum quantity as follows:

MEDICINAL PRODUCT medicinal product pack	**PBS item code**	**Max. qty packs**	**Max. qty units**	**№.of Rpts**	**Available brands**
TRIGLYCERIDES LONG CHAIN WITH GLUCOSE POLYMER					
triglycerides long chain with glucose polymer oral liquid, 6 x 1 L cartons	9309Y	3	3	5	ProZero
Restriction Summary [new] / Treatment of Concept: [new]					
	Category / Program: ☒ GENERAL - General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners ☒Nurse practitioners				
	Restriction type: ☒Restricted benefit				
	Indication: Proven inborn errors of protein metabolism				
	Clinical criteria:				
	Patient must be unable to meet their energy requirements with permitted food and formulae				

These restrictions may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

8 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.

9 Sponsor's Comment

The sponsor had no comment.