

5.24 SEVELAMER

Powder for oral liquid, 2.4g (as sevelamer carbonate), Renvela[®], Sanofi-Aventis Australia Pty Ltd

1 Purpose of Application

- 1.1 The minor submission requested for a General Schedule and Section 100 (Highly Specialised Drugs Program – Public and Private Hospital) listing of sevelamer carbonate, as powder for suspension, for hyperphosphataemia in patients undergoing dialysis for chronic kidney disease.

2 Requested listing

- 2.1 The minor submission requested for the PBS listing of a new form of sevelamer (as sevelamer carbonate), with the same indications and restrictions as sevelamer (as sevelamer hydrochloride) 800 mg tablets currently listed on the PBS.
- 2.2 Suggestions and additions proposed by the Secretariat to the requested listing are added in italics and suggested deletions are crossed out with strikethrough:

Name, Restriction, Manner of administration and form	Max. Qty (Packs)	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
SEVELAMER <i>Sevelamer carbonate, powder for oral liquid, 2.4g, 60</i>	1	5	\$332.52	Renvela® Sanofi-Aventis Australia 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			
Episodicity:	Chronic therapy			
Severity:	Severe			
Condition:	Hyperphosphataemia in adult patients with stage 4 and 5 chronic kidney disease			
PBS Indication:	Hyperphosphataemia			
Treatment phase:	Maintenance following initiation and stabilisation			
Restriction Level / Method:	<input 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 checked="" type="checkbox"/> Streamlined			
Treatment criteria:	Patient must be undergoing dialysis for chronic kidney disease.			

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Clinical criteria:	The condition must not be adequately controlled by calcium, AND Patient must have a serum phosphate of greater than 1.6 mmol per L at the commencement of therapy; OR The condition must be where a serum calcium times phosphate product is greater than 4 at the commencement of therapy, AND The treatment must not be used in combination with any other non-calcium phosphate binding agents
Population criteria:	Patient must be 18 years old and over

Name, Restriction, Manner of administration and form	Max. Qty (Packs)	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
SEVELAMER Sevelamer carbonate, powder for oral liquid, 2.4g, 60	1	5	\$589.00 (Public) \$619.71 (Private)	Renvela® Sanofi-Aventis Australia Pty Ltd
Category / Program	Section 100 – Highly Specialised Drugs Program (Public and Private)			
Prescriber type:	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives			
Episodicity:	Chronic therapy			
Severity:	Severe			
Condition:	Hyperphosphataemia in adult patients with stage 4 and 5 chronic kidney disease			
PBS Indication:	Hyperphosphataemia			
Treatment phase:	Initiation and stabilisation			
Restriction Level / Method:	<input 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 checked="" type="checkbox"/> Streamlined			
Treatment criteria:	Patient must be undergoing dialysis for chronic kidney disease.			
Clinical criteria:	The condition must not be adequately controlled by calcium, AND Patient must have a serum phosphate of greater than 1.6 mmol per L at the commencement of therapy; OR The condition must be where a serum calcium times phosphate product is greater than 4 at the commencement of therapy, AND The treatment must not be used in combination with any other non-calcium phosphate binding agents.			
Population criteria:	Patient must be 18 years old and over			

For more detail on PBAC's view, see Section 5 PBAC outcome.

3 Background

3.1 TGA status at time of PBAC consideration: Sevelamer carbonate powder for suspension is ARTG registered for the management of hyperphosphataemia in adult patients with stage 4 and 5 chronic kidney disease.

- 3.2 Sevelamer carbonate has not previously been considered by the PBAC.
- 3.3 Sevelamer is currently available on the PBS as sevelamer hydrochloride 800 mg tablets for hyperphosphataemia in patients undergoing dialysis for chronic kidney disease.
- 3.4 The minor submission claimed that sevelamer carbonate powder for suspension may help reduce the pill burden in patients with chronic kidney disease, or as an alternative dose form for patients who have difficulty swallowing the sevelamer hydrochloride tablets.

For more detail on PBAC's view, see Section 5 PBAC outcome.

4 Consideration of the evidence

Sponsor hearing

- 4.1 There was no hearing for this item as it was a minor submission.

Consumer comments

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

Clinical Evidence

- 4.3 The TGA-approved Australian Product Information (PI) indicated that the recommended dosage of the 2.4 g powder for suspension of sevelamer carbonate is with each meal, three times a day, resulting in a daily administration of up to 7.2 g (2.4 g x 3) of powder for suspension. However, the PI also recommended a starting dose of between 2.4 g to 4.8 g per day.
- 4.4 The submission stated that two of the efficacy and safety cross over studies considered by the TGA were relevant to support the PBS listing of sevelamer carbonate on a cost-minimisation basis to sevelamer hydrochloride (Study SVCARB00205 and Study GD3-163-201). The Pre-PBAC response (p1) clarified that although not implicitly stated, the submission sought for price parity on the basis of a per milligram equivalence.

These studies directly compared the efficacy and safety between sevelamer carbonate (as tablets or powder for suspension) and sevelamer hydrochloride (as tablets) given TDS with meals in hyperphosphatemic patients with CKD. Study GD3-119-301, which was included in the TGA dossier may also be relevant to establishing the equivalence of sevelamer hydrochloride and sevelamer carbonate. The submission excluded this study on the grounds that it compared once daily sevelamer carbonate dosing with thrice daily sevelamer hydrochloride dosing. The Pre-PBAC response (p2) maintained that it was inappropriate to include this study in the comparison as it did not result in comparable serum phosphate levels and a once daily dosing regimen was not recommended by the TGA.

- 4.5 The TGA approved PI stated that the average actual daily doses in these three studies were:
- GD3-163-201 (cross-over study of sevelamer carbonate 800 mg tablets and sevelamer hydrochloride 800 mg tablets): 6.0 g/day for both treatments.
 - SVCARB00205 (cross-over study of sevelamer carbonate powder and sevelamer hydrochloride tablets): 6.0 g/day and 6.4 g/day of sevelamer carbonate powder and sevelamer hydrochloride tablets, respectively.
 - GD3-199-301 (sevelamer carbonate powder once daily and sevelamer hydrochloride tablets thrice daily): 6.2 g/day and 6.7 g/day of sevelamer carbonate powder and sevelamer hydrochloride tablets, respectively.
- 4.6 The TGA product information “Dosage and Administration” for sevelamer carbonate states that:
- “The recommended starting dose of sevelamer carbonate is 2.4 to 4.8 g per day based on clinical needs and phosphorus level. Sevelamer carbonate must be taken three times per day with meals.”
 - “In clinical practice, treatment will be continuous based on the need to control serum phosphorus levels and the daily dose is expected to be an average of approximately 6 g per day”.
- 4.7 The TGA has registered sevelamer carbonate in strengths of 1.6 g and 2.4 g. However, the submission requested for PBS listing of the 2.4 g strength of sevelamer carbonate alone, dose titration as recommended by the PI would not be feasible in practice. The Pre-PBAC response (p2) argued that the 2.4 g strength of sevelamer carbonate alone was the dose most relevant for the requested PBS population.
- 4.8 In contrast, the currently listed presentation of sevelamer hydrochloride 800 mg tablets allows the dose to be titrated in 800 mg increments.
- 4.9 Furthermore, as the clinical studies demonstrate that an average daily dose of 6g was adequate, the submission’s proposal of a daily dose of 7.2 g (2.4 g powder taken thrice daily), was not consistent with the clinical evidence or the TGA approved PI. The Pre-PBAC response (p 2-3) argued that this assumption was inappropriate, as the 6 g average daily dose in the trials was a result of approximately 85% compliance of the proposed daily prescribed dose of 7.2 g. The PBAC noted that the TGA nonetheless considered it appropriate for the Product Information to indicate that the average dose daily dose was 6 g, and that this dose could not be achieved with the 2.4 g powder.
- 4.10 The minor submission proposed an ex-manufacturer price of \$294.50 for 1 pack of sevelamer carbonate 2.4 g containing 60 sachets, which is an equivalent price per mg to one pack of 800 mg sevelamer hydrochloride containing 180 tablets.
- 4.11 However, since the clinical studies presented in the submission and included in the PI demonstrated that an average daily dose of 6 g was adequate, the PBAC considered the proposed ex-manufacturer price should be adjusted (i.e. \$ [REDACTED] =

\$294.50/) to account for the additional dosing that would be inevitable if the requested presentation was PBS-listed, but that may not provide additional clinical benefit, or, for the situation in which the patient discards part of the contents of a sachet in order to achieve the desired dose.

Estimated PBS usage & financial implications

- 4.12 The minor submission claimed that the listing of sevelamer carbonate 2.4 g powder for suspension would be cost-neutral to the Commonwealth, noting that neither the expected clinical outcome nor the population for sevelamer would change as a result of this PBS listing. It is possible that the cost to the PBS will be increased by the listing of sevelamer carbonate as the lack of ability to finely titrate doses with this presentation means that patients could be treated with higher doses than are required, or discard partial doses.

For more detail on PBAC's view, see Section 5 PBAC outcome.

5 PBAC Outcome

- 5.1 The PBAC recommended the General Schedule and Section 100 (Highly Specialised Drugs Program – Public and Private Hospital) Authority Required listing of sevelamer carbonate, as powder for suspension, for hyperphosphataemia in patients undergoing dialysis for chronic kidney disease. In making this recommendation, the PBAC considered that the PBS listing of this formulation could potentially reduce the pill burden for these patients, but advised the Minister that a lower price for sevelamer carbonate should be negotiated to take into account the Committee's concerns regarding the higher doses without additional clinical benefit and/or wastage upon administration of this strength of sevelamer carbonate.
- 5.2 The PBAC considered that the proposed restriction was appropriate, noting that it was similar to the current PBS listing for sevelamer hydrochloride tablets. The PBAC advised that episodicity, severity and condition requiring the indication to be 'chronic' and of a 'severe' nature in 'adult patients with stage 4 and 5 chronic kidney disease', respectively, be removed from the indication to maintain consistency with the current PBS listing for sevelamer hydrochloride tablets.
- 5.3 The PBAC noted that the TGA-approved Australian PI recommends sevelamer carbonate be taken three times per day with meals at a dosage based on individual patient requirements to control phosphate levels. The PBAC further noted that the PI also recommends a starting dose of between 2.4 g to 4.8 g per day and states that in clinical practice, treatment will be continuous and the daily dose is expected to be an average of approximately 6 g per day.
- 5.4 The PBAC noted that although a 1.6 g strength of sevelamer carbonate powder for suspension was registered in Australia, PBS listing was only sought for the 2.4 g strength of the formulation. The PBAC did not accept the argument in the Pre-PBAC response (p2) stating that the 2.4 g strength sevelamer carbonate alone was the dose most relevant for the requested PBS population.

- 5.5 The PBAC noted that while the currently listed presentation of sevelamer hydrochloride 800 mg tablets allows the dose to be titrated in 800 mg increments, 7.2 g of sevelamer carbonate (2.4 g powder taken thrice daily) could lead to a 1.2 g excessive dose to clinical need, and/or wastage in the context of an expected average dose of 6 g per day.
- 5.6 The PBAC considered that the long-term impact of additional dosing of sevelamer carbonate was unclear, noting that the TGA Delegate’s overview stated that “[l]ong term clinical trial efficacy data has not been submitted in support of the sevelamer carbonate salt however, by demonstrating therapeutic equivalence between sevelamer hydrochloride and sevelamer carbonate, the efficacy over years based on sevelamer hydrochloride has been extrapolated. This is acceptable because the studies were conducted in sufficiently similar patient populations in terms of baseline demographics and underlying disease processes, with similar efficacy endpoints.”
- 5.7 The PBAC advised that sevelamer carbonate should not be exempt from the Early Supply Rule, as it applies to the current PBS listing for sevelamer hydrochloride.
- 5.8 The PBAC advised that sevelamer carbonate is suitable for prescribing by nurse practitioners, in the maintenance phase, following stabilisation.
- 5.9 The PBAC advised that this submission it would not meet the criteria for an Independent Review as it is for a new form of a currently listed drug.

Outcome:

Recommended

6 Recommended listing

Add new item:

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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			
PBS Indication:	Hyperphosphataemia			
Treatment phase:	Maintenance following initiation and stabilisation			

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Restriction Level / Method:	<input 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 checked="" type="checkbox"/> Streamlined
Treatment criteria:	Patient must be undergoing dialysis for chronic kidney disease.
Clinical criteria:	The condition must not be adequately controlled by calcium, AND Patient must have a serum phosphate of greater than 1.6 mmol per L at the commencement of therapy; OR The condition must be where a serum calcium times phosphate product is greater than 4 at the commencement of therapy, AND The treatment must not be used in combination with any other non-calcium phosphate binding agents
Population criteria:	Patient must be 18 years old and over

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PBS Indication:	Hyperphosphataemia			
Treatment phase:	Initiation and stabilisation			
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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.