

14.03(b) SEVELAMER

Tablet containing sevelamer carbonate 800 mg Sevelamer Dr Reddy's[®], Dr Reddy's Laboratories (Australia) Pty Ltd

1 Purpose of Application

- 1.1 The minor submission requested a General Schedule listing and a Section 100 (Highly Specialised Drugs) listing of Sevelamer Dr Reddy's (tablet containing sevelamer carbonate), for the management of hyperphosphataemia in patients with chronic kidney disease that require dialysis.

2 Requested listing

- 2.1 The submission requested a new listing for Sevelamer Dr Reddy's (tablet containing sevelamer carbonate), with the same indication and restriction as sevelamer hydrochloride 800 mg (Renagel[®]) that is currently listed on the PBS.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Manufacturer	Name and
SEVELAMER Sevelamer carbonate, tablet 800, mg, 180	1	5	\$229.98	Sevelamer Dr Reddy's	
				Dr Reddy's Laboratories Australia Pty Ltd	

Category / Program	GENERAL – General Schedule (Code GE)
Prescriber type:	<input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners
PBS Indication:	Hyperphosphataemia
Treatment phase:	Maintenance following initiation and stabilisation
Restriction Level / Method:	<input type="checkbox"/> Authority Required - In Writing <input type="checkbox"/> Authority Required - Telephone <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.
Administrative Advice	Shared Care Model: For prescribing by nurse practitioners where care of a patient is shared between a nurse practitioner and medical practitioner in a formalised arrangement with an agreed management plan. Further information can be found in the Explanatory Notes for Nurse Practitioners.

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
SEVELAMER Sevelamer carbonate, tablet 800, mg, 180	2	5	\$530.10 (HSD Public) \$558.59 (HSD Private)	Sevelamer Dr Reddy's Dr Reddy's Laboratories Australia Pty Ltd

Category / Program	Section 100 – Highly Specialised Drugs Program (Public and Private Hospitals)
Prescriber type:	<input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners
PBS Indication:	Hyperphosphataemia
Treatment phase:	Maintenance following initiation and stabilisation
Restriction Level / Method:	<input checked="" type="checkbox"/> Authority Required – Telephone (Private Hospitals) <input checked="" type="checkbox"/> Streamlined (Public Hospitals)
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.

Administrative Advice	<p>Shared Care Model:</p> <p>For prescribing by nurse practitioners where care of a patient is shared between a nurse practitioner and medical practitioner in a formalised arrangement with an agreed management plan. Further information can be found in the Explanatory Notes for Nurse Practitioners.</p>
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For more detail on PBAC’s view, see section 6 PBAC outcome.

3 Background

- 3.1 Sevelamer Dr Reddy’s (sevelamer carbonate 800 mg) has TGA registration for the management of hyperphosphataemia in adult patients with stage 4 and 5 chronic kidney disease.
- 3.2 Sevelamer carbonate 2.4g as a powder for suspension (Renvela®) sponsored by Sanofi-Aventis was recommended by the PBAC for the same indication (PBAC November 2017). To date, Sanofi has not proceeded with this listing on the PBS.
- 3.3 Sevelamer is currently available on the PBS as sevelamer hydrochloride 800 mg tablets (Renagel®) for the management of hyperphosphataemia in patients undergoing dialysis for chronic kidney disease.

For more detail on PBAC’s view, see section 6 PBAC outcome.

4 Consideration of the evidence

Clinical trials

- 4.1 The TGA has previously considered Renagel and sevelamer carbonate (Renvela) salts to have a favourable benefit risk profile in adult patients with stage 4 and 5 chronic renal disease. The TGA based this conclusion on therapeutic equivalence evidenced from extensive worldwide post marketing experience, long established use in clinical practice in Australia and safety profile based on estimated cumulative exposure of 1.9 million patient years for both the salts¹.
- 4.2 The submission presented one in vitro equilibrium binding and kinetic study (VP15151) to demonstrate bioequivalence between 800 mg tablets of sevelamer Dr Reddy’s and Renvela.

Table 1: Trials and associated reports presented in the submission

Trial ID/First Author	Protocol title/ Publication title	Publication citation
Bioequivalence studies		
VP15151	In-Vitro Bioequivalence study of sevelamer carbonate tablets 800 mg (biostatistical component)	Unpublished

Source: Attachment 3 to the submission.

¹ Therapeutic Goods Administration, AusPAR Renvela / Sevelamer Carbonate Winthrop/ Sevelamer carbonate Sanofi, Sanofi Aventis Australia Pty Ltd 2015

- 4.3 Additionally, the submission also referenced results presented in the Australian Public Assessment Record (AusPAR) for sevelamer carbonate (2015) for two other studies:
- an in vitro equilibrium binding and kinetic study (TR-2527-07-SC) to demonstrate bioequivalence between Renegel 800 mg tablets and Renvela 800 mg tablets; and
 - a phase II, randomised, double-blind cross-over therapeutic equivalence study (n=78) comparing Renegel with Renvela (GD3-163-201).
- 4.4 The submission claims that Sevelamer Dr Reddy's and Renegel are bioequivalent referring to the studies cited at 4.2 and 4.3 and TGA advice that Sevelamer Dr Reddy's and Renvela were therapeutically equivalent (and bioequivalent).
- 4.5 The TGA has also noted that Renvela and Renegel are known to have different safety profiles. The current submission to PBAC concluded that there were no marked differences in the treatment related adverse event profiles of Renvela and Renegel based on results from GD3-163-201. The pre-PBAC response commented on the safety profiles of sevelamer hydrochloride and sevelamer carbonate, noting that the main risks of treatment is the onset of gastrointestinal adverse events including nausea and vomiting. The pre-PBAC response noted that the two salts in tablet form to have similar safety profiles at the proposed dosage regimen of two tablets three times daily (TDS).

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

5 Estimated PBS usage & financial implications

- 5.1 The minor submission estimated there to be no financial implications to the PBS as the submission expected sevelamer carbonate to only substitute for sevelamer hydrochloride (Renegel), and both products would have the same price.
- 5.2 Whilst not a matter for PBAC, the proposed listing would trigger a statutory price reduction under Section 99ACB of the Act.

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

6 PBAC Outcome

- 6.1 The PBAC recommended the listing of a new form of sevelamer (Sevelamer Dr Reddy's) for the treatment of hyperphosphataemia. The PBAC's recommendation for listing was based, among other matters, on its assessment that on a per gram basis Sevelamer Dr Reddy's is equi-effective to Renegel.
- 6.2 The PBAC considered the claim that Sevelamer Dr Reddy's is therapeutically equivalent (and bioequivalent) to Renegel was reasonable based on the studies presented in the submission.
- 6.3 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.
- 6.4 The PBAC advised that sevelamer carbonate is suitable for prescribing by nurse practitioners under a shared care arrangement, in the maintenance phase, following stabilisation.

- 6.5 The PBAC advised, under Section 101 (4AACD) of the *National Health Act 1953*, that the Sevelamer Dr Reddy's and Renagel should be considered equivalent for the purposes of substitution (i.e., 'a' flagged in the Schedule with a NOTE stating PBS of one form and PBS of another form are equivalent for the purposes of substitution).
- 6.6 The PBAC noted this submission was not eligible for an Independent Review, as it received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

Add new item:

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer
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Administrative Advice	<p>Shared Care Model:</p> <p>For prescribing by nurse practitioners where care of a patient is shared between a nurse practitioner and medical practitioner in a formalised arrangement with an agreed management plan. Further information can be found in the Explanatory Notes for Nurse Practitioners.</p> <p>Pharmaceutical benefits that have the forms sevelamer hydrochloride 800 mg and sevelamer carbonate 800 mg tablet are equivalent for the purposes of substitution</p>
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Name, Restriction, Manner of administration and form	Max. Qty	No.of Rpts	Proprietary Name and Manufacturer
SEVELAMER Sevelamer carbonate, tablet 800, mg, 180	2	5	Sevelamer Dr Reddy's Dr Reddy's Laboratories Australia Pty Ltd

Category / Program	Section 100 – Highly Specialised Drugs Program (Public and Private Hospitals)
Prescriber type:	<input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners
PBS Indication:	Hyperphosphataemia
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Administrative Advice	<p>Shared Care Model:</p> <p>For prescribing by nurse practitioners where care of a patient is shared between a nurse practitioner and medical practitioner in a formalised arrangement with an agreed management plan. Further information can be found in the Explanatory Notes for Nurse Practitioners.</p> <p>Pharmaceutical benefits that have the forms sevelamer hydrochloride 800 mg and sevelamer carbonate 800 mg tablet are equivalent for the purposes of substitution</p>

8 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.

9 Sponsor's Comment

The sponsor had no comment.