

## 5.12 CINACALCET

Tablet 30 mg,

Tablet 60 mg,

Tablet 90 mg,

Pharmacor Cinacalcet<sup>®</sup>,

Pharmacor Pty Limited.

### 1 Purpose of Application

- 1.1 The minor submission requested the listing of cinacalcet for the treatment of secondary hyperparathyroidism (SHPT) in patients with chronic kidney disease (CKD) receiving dialysis.

### 2 Requested listing

- 2.1 The requested restrictions are presented below. Suggestions and additions to the requested listing proposed by the Secretariat and the PBAC were added in italics and suggested deletions were crossed out with strikethrough.

#### Listing 1. HSD Private/Public Hospital – Initiation

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Manufacturer	Name and
CINACALCET HYDROCHLORIDE					
Tablet ( <del>film-coated</del> ), 30 mg, 28	2	5	\$ [REDACTED] (Public Hospital)	Pharmacor Cinacalcet Tablets	Pharmacor Pty Ltd
			\$ [REDACTED] (Private Hospital)		
Tablet ( <del>film-coated</del> ), 60 mg, 28	2	5	\$ [REDACTED] (Public Hospital)		
			\$ [REDACTED] (Private Hospital)		
Tablet ( <del>film-coated</del> ), 90 mg, 28	2	5	\$ [REDACTED] (Public Hospital)		
			\$ [REDACTED] (Private Hospital)		

<b>Category / Program:</b>	Section 100 – Highly Specialised Drugs Program (Private Hospital) Section 100 – Highly Specialised Drugs Program (Public Hospital)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Condition:</b>	Secondary hyperparathyroidism
<b>PBS Indication:</b>	<del>Management, including initiation and stabilisation, of sustained secondary hyperparathyroidism not responding to conventional therapy. Secondary hyperparathyroidism</del>
<b>Treatment phase:</b>	Initial
<b>Restriction Level / Method:</b>	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required – In Writing <input checked="" type="checkbox"/> Authority Required – Telephone/Electronic/Emergency <input type="checkbox"/> Streamlined
<b>Treatment criteria:</b>	Must be treated by a nephrologist

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<b>Clinical criteria:</b>	<p>The patient must have chronic kidney disease  <b>AND</b>  <i>The patient must be on dialysis</i>  <b>AND</b>  <i>The patient must not have responded to conventional therapy</i>  <b>AND</b>  <i>The patient must have sustained hyperparathyroidism with iPTH of at least 50 pmol per L</i>  <b>OR</b>  <i>The patient must have sustained hyperparathyroidism with iPTH of at least 15 pmol per L and less than 50 pmol per L AND an (adjusted) serum calcium concentration at least 2.6 mmol per L</i></p> <p><del>Note: "Sustained" means the abnormality was detected on at least 2 blood samples collected over a period of 2 to 4 months.</del></p>
<b>Prescriber Instructions:</b>	<p>During the titration phase, intact PTH should be monitored 4 weekly (measured at least 12 hours post dose) and dose titrated until an appropriate iPTH concentration is achieved. During the titration phase, approval will be limited to sufficient supply for supply for 4 weeks treatment at a time, with doses between 30 and 180 mg per day according to the patient's response and tolerability.</p>
<b>Administrative Advice:</b>	<p><del>"Sustained" means the abnormality was detected on at least 2 blood samples collected over a period of 2 to 4 months.</del></p>

**Listing 2. HSD Private/Public Hospital – Continuation**

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary and Manufacturer	Name
CINACALCET HYDROCHLORIDE					
Tablet (film-coated), 30 mg, 28	2	5	\$ [REDACTED] (Public Hospital) \$ [REDACTED] (Private Hospital)	Pharmacor	Pharmacor Pty Ltd
Tablet (film-coated), 60 mg, 28	2	5	\$ [REDACTED] (Public Hospital) \$ [REDACTED] (Private Hospital)	Cinacalcet Tablets	
Tablet (film-coated), 90 mg, 28	2	5	\$ [REDACTED] (Public Hospital) \$ [REDACTED] (Private Hospital)		

<b>Category / Program:</b>	Section 100 – Highly Specialised Drugs Program (Private Hospital) Section 100 – Highly Specialised Drugs Program (Public Hospital)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Condition:</b>	Secondary hyperparathyroidism
<b>PBS Indication:</b>	<del>Management, including initiation and stabilisation, of sustained secondary hyperparathyroidism not responding to conventional therapy. Secondary hyperparathyroidism</del>
<b>Treatment phase:</b>	Continuing
<b>Restriction Level / Method:</b>	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required – In Writing <input type="checkbox"/> Authority Required – Telephone/Electronic/Emergency <input checked="" type="checkbox"/> Streamlined
<b>Treatment criteria:</b>	Must be treated by a nephrologist

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<b>Clinical criteria:</b>	The patient must have chronic kidney disease <b>AND</b> The patient must be on dialysis <b>AND</b> The patient must have previously received PBS-subsidised cinacalcet therapy treatment with this drug for this condition Note: "Sustained" means the abnormality was detected on at least 2 blood samples collected over a period of 2 to 4 months.
<b>Prescriber Instructions:</b>	During the titration phase, intact PTH should be monitored 4 weekly (measured at least 12 hours post dose) and dose titrated until an appropriate iPTH concentration is achieved. During the titration phase, approval will be limited to sufficient supply for supply for 4 weeks treatment at a time, with doses between 30 and 180 mg per day according to the patient's response and tolerability. During the maintenance phase, approval will be limited to provide sufficient quantity for 4 weeks treatment up to a maximum of 6 months supply for doses between 30 and 180 mg per day according to the patient's response and tolerability. Intact PTH should be monitored quarterly (measured at least 12 hours post dose) and dose adjusted as necessary to maintain an appropriate iPTH concentration.
<b>Administrative Advice:</b>	"Sustained" means the abnormality was detected on at least 2 blood samples collected over a period of 2 to 4 months.

**Listing 3. General Schedule – Continuation only**

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Dispensed Price for Max. Qty	Proprietary Name and Manufacturer
CINACALCET HYDROCHLORIDE				
Tablet (film-coated), 30 mg, 28	1	5	\$ [REDACTED]	Pharmacor
Tablet (film-coated), 60 mg, 28	1	5	\$ [REDACTED]	Cinacalcet Tablets Pty Ltd
Tablet (film-coated), 90 mg, 28	1	5	\$ [REDACTED]	

<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>	Secondary hyperparathyroidism
<b>PBS Indication:</b>	Maintenance therapy, following initiation and stabilisation of treatment with cinacalcet for sustained secondary hyperparathyroidism. Secondary hyperparathyroidism
<b>Treatment phase:</b>	Continuing
<b>Restriction Level / Method:</b>	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required – In Writing <input type="checkbox"/> Authority Required – Telephone/Electronic/Emergency <input checked="" type="checkbox"/> Streamlined
<b>Clinical criteria:</b>	The patient must have chronic kidney disease <b>AND</b> The patient must be on dialysis <b>AND</b> The patient must have had a decrease of at least 30% in iPTH concentrations after 6 months treatment <b>OR</b> The patient must have had iPTH greater than 15 pmol per L and an (adjusted) serum calcium concentration of less than 2.6 mmol per L after 6 months treatment

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<b>Prescriber Instructions:</b>	<p>During the titration phase, intact PTH should be monitored 4 weekly (measured at least 12 hours post dose) and dose titrated until an appropriate iPTH concentration is achieved. During the titration phase, approval will be limited to sufficient supply for 4 weeks treatment at a time, with doses between 30 and 180 mg per day according to the patient's response and tolerability.</p> <p>During the maintenance phase, approval will be limited to provide sufficient quantity for 4 weeks treatment up to a maximum of 6 months supply for doses between 30 and 180 mg per day according to the patient's response and tolerability.</p> <p>Intact PTH should be monitored quarterly (measured at least 12 hours post dose) and dose adjusted as necessary to maintain an appropriate iPTH concentration.</p>
<b>Administrative Advice:</b>	<p>Continuing Therapy Only:</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>

- 2.2 The submission requested the same listing as Sensipar® brand of cinacalcet (Sensipar from herein; sponsored by Amgen Australia Pty Ltd) when it was previously listed on the PBS.
- 2.3 At the November 2007 meeting, the PBAC recommended that cinacalcet should be listed in Section 85 for maintenance treatment as suggested by the Australian and New Zealand Society of Nephrology, to enable patients in rural areas easier access to continuing treatment (Cinacalcet November 2007 Public Summary Document (PSD)). The submission noted that there was a high proportion of patients within the Aboriginal and Torres Strait Islander population who were on dialysis but would be less likely to receive a kidney transplant compared to non-Indigenous people.
- 2.4 The approved Product Information stated that the recommended starting dose is 30mg once daily titrated every 2-4 weeks to a maximum dose of 180mg once daily to achieve a target parathyroid hormone (PTH) between 1.5-5 times upper limit of normal. Tablets are administered orally and are taken whole and should not be divided. The initial and continuing Section 100 listings requested a maximum quantity of 2 packs of 28 tablets, with a maximum of 5 repeats. The continuing listing under Section 85 requested a maximum quantity of 1 pack of 28 tablets, with a maximum of 5 repeats. The Pre-PBAC response specified that the proposed maximum quantities and repeats were based on those applying to Sensipar prior to delisting, and noted that the 4 weekly monitoring requirement may not apply following stabilisation on maintenance therapy under Section 85 listing. The suggestion for 5 repeats in this phase was to provide a suitable duration of therapy and patients still being stabilised or titrated can be prescribed smaller quantities under the discretion of the prescriber. The PBAC considered the maximum quantity and repeats requested were appropriate. The PBAC also agreed that the 4 weekly monitoring criterion in the Prescriber Instructions could be removed in the continuing treatment restrictions.
- 2.5 The previous listing of cinacalcet had a Special Pricing Arrangement (SPA), however the Pre-PBAC response indicated that an SPA for this submission would be unlikely.

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

### **3 Background**

- 3.1 Pharmacor Cinacalcet was ARTG listed on 8 January 2019 based on the TGA being satisfied that it was bioequivalent to Sensipar. Both brands of cinacalcet have the following TGA-approved indications:
- Cinacalcet may be used to treat the biochemical manifestations of secondary hyperparathyroidism in patients with end stage renal disease, receiving dialysis. Cinacalcet should be used as adjunctive therapy.
  - Cinacalcet is indicated for the treatment of hypercalcemia in patients with parathyroid carcinoma.
  - Cinacalcet may be used to treat the biochemical manifestations of primary hyperparathyroidism in patients for whom parathyroidectomy is not a treatment option.
- 3.2 This is the first time PBAC has considered a submission for cinacalcet under the brand name Pharmacor Cinacalcet. However, cinacalcet has previously been considered by the PBAC.
- 3.3 Sensipar was PBS listed from 1 July 2008 to 31 July 2015 for the treatment of sustained hyperparathyroidism in patients with CKD on dialysis, not responding to conventional therapy.
- 3.4 At its November 2007 meeting, the PBAC recommended the listing of Sensipar for the treatment of SHPT in patients with end stage renal disease receiving dialysis on the basis of acceptable cost-effectiveness compared with placebo. This recommendation was based on a meta-analysis of five biomarker randomised controlled trials (RCTs) which suggested that treatment with cinacalcet was associated with changes in intact-parathyroid hormone (iPTH) levels and subsequent reductions in parathyroidectomies, cardiovascular-related hospitalisations and fractures compared to placebo. The PBAC recommended a risk-sharing arrangement (RSA) which required the Sponsor provide all ongoing data to the Commonwealth on the efficacy and cost-effectiveness of the drug.
- 3.5 At its November 2013 meeting, the PBAC considered a submission where the Sponsor for Sensipar provided the results of the EVOLVE clinical trial to address the requirements of the RSA for Sensipar. Based on the evidence provided in the submission, the PBAC considered all ICER figures far exceeded the original ratio of between \$15,000 and \$45,000 per QALY gained that enabled the PBAC to recommend the PBS listing of cinacalcet in 2007. Therefore, the PBAC made a new recommendation that based upon the new evidence from the EVOLVE trial, at the current price, cinacalcet was not cost-effective. The PBAC considered that a significant price reduction would be needed to restore the cost-effectiveness of cinacalcet to the level considered to be acceptable in 2007.

- 3.6 At its March 2014 meeting, the PBAC considered a submission in response to the November 2013 decision where the Sponsor for Sensipar requested to vary the current restriction criteria to align with Kidney Disease: Improving Global Outcomes (KDIGO) Guidelines to revise the price offer. In terms of the pricing proposal, the PBAC rejected the Sponsor's price offer, considering that the price reduction offered was not sufficient to restore the cost-effectiveness of cinacalcet. The PBAC reaffirmed its advice of November 2013 that, at its current price, cinacalcet was not cost effective. The PBAC advised that it would remain open to the Sponsor to make a future submission to demonstrate that cinacalcet is cost-effective, including by targeting further a listing for the patient group that is most likely to benefit from treatment with cinacalcet. However, the mere potential for such a submission to be made in the future, would not justify the government continuing to pay a higher subsidy in the meantime (cinacalcet PSD March 2014).
- 3.7 On 1 September 2014, the published price of cinacalcet was reduced.
- 3.8 A major submission for Sensipar was made to the PBAC to be considered at the November 2014 meeting, requesting to amend the existing restriction to target patients with chronic kidney disease who are at high risk of cardiovascular events. This submission was withdrawn by the Sponsor before being considered by the PBAC.
- 3.9 Sensipar was de-listed from the PBS on 1 August 2015.

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

## **4 Population and disease**

- 4.1 SHPT is one of the principle manifestations of CKD. It is a metabolic condition that is characterised by the excessive secretion of parathyroid hormone (PTH) by the parathyroid glands in an attempt to regulate calcium and phosphate levels as the kidney fails. SHPT is associated with an increase in cardiovascular events, pathological fractures and overall mortality in patients with CKD. (Cinacalcet PSD November 2013). If standard treatment fails, parathyroidectomy surgery is the next alternative therapy however is not suitable for all patients and is associated with adverse outcomes such as risk of re-hospitalisation with hypocalcaemia.
- 4.2 Cinacalcet is a calcimimetic agent that increases the sensitivity of the calcium sensing receptor to extracellular calcium. Cinacalcet reduces PTH while simultaneously lowering serum calcium and phosphorus levels in CKD in patients receiving dialysis.
- 4.3 The submission claimed that the removal of cinacalcet from the PBS created an unmet clinical need for certain patients. The submission also claimed that based on a number of Australian observational studies there has been an increase in parathyroidectomy surgery rates due to the unavailability of cinacalcet. Sensipar is currently available on the private market in Australia. There is currently no specific alternative calcimimetic available on the PBS for patients with CKD receiving dialysis with SHPT.

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

## 5 Comparator

- 5.1 The submission did not nominate a comparator. The submission noted that the comparator in all SHPT submissions accepted by the PBAC was placebo for add-on to standard medical management involving dietary modification, vitamin D products in association with calcium-based phosphate binders and dialysate-based interventions. The submission proposed that the listing and pricing arrangement for cinacalcet be consistent with the previous listing for Sensipar.

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

## 6 Consideration of the evidence

### ***Sponsor hearing***

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

### ***Consumer comments***

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

### ***Interpretation of clinical evidence***

- 6.3 The submission presented the EVOLVE trial data, which was also presented in the November 2013 Sensipar submission.
- 6.4 As noted in November 2013, the EVOLVE trial was an international, randomised, double-blind trial comparing the effects of cinacalcet and placebo on mortality and cardiovascular morbidity in dialysis patients with SHPT (n=3,883) (cinacalcet PSD November 2013).
- 6.5 At the November 2013 PBAC meeting, the Sensipar submission claimed that based on the EVOLVE trial, cinacalcet was superior in terms of efficacy and inferior in terms of safety compared to placebo (standard medical management). The PBAC disagreed with the clinical claims because the EVOLVE trial did not demonstrate a statistically significant difference over placebo in the primary outcome, and there was a higher incidence of adverse events with cinacalcet. The PBAC considered that the only benefit that was consistently observed with cinacalcet treatment was a reduction in parathyroidectomy. (Cinacalcet PSD November 2013).
- 6.6 The current submission noted that there were a number of key issues with the EVOLVE study design and analysis, which resulted in the study being underpowered to detect a treatment difference between cinacalcet and placebo. Overall, the submission claimed the EVOLVE trial showed the effectiveness of cinacalcet in the relevant PBS population. The submission claimed that the failure to demonstrate a mortality difference in the EVOLVE trial was due to the trial design rather than the ineffectiveness of cinacalcet.

- 6.7 Additionally, the Pre-PBAC response noted that in the pre-specified subgroup analyses, there was a significant effect on the primary composite outcome seen in older patients aged  $\geq 65$  years (relative hazard 0.74; 95%CI 0.63, 0.86 (*p-interaction* = 0.01). The Pre-PBAC response claimed that since patients in this age group were likely to be unsuitable for parathyroidectomy and that cinacalcet would be the likely treatment option for SHPT.
- 6.8 The submission also presented four Australian retrospective observational studies that investigated the clinical impact of de-listing cinacalcet from the PBS. The submission provided the following summary:
- All studies included patients with CKD receiving dialysis, which is consistent with the PBS population for cinacalcet.
  - The largest study (n=228) had a mean age of 63 years old (Ruderman et al., 2019). Another study (n=195) had a median age of 57 (van der Plas et al., 2019). No patient characteristics were provided for the two smaller studies.
  - There were significant increases in serum PTH, calcium and alkaline phosphatase over a 12-month period following withdrawal (Ruderman et al., 2019).
  - All studies showed an increased rate of parathyroidectomy post delisting. The submission reported that a number of adverse outcomes seen with parathyroidectomies in patients on dialysis included 2% 30-day mortality rate and 23.8% re-hospitalisation rate in the year following surgery, with a greater risk of morbidity and mortality seen in older patients (Ishani et al., 2015). The PBAC noted that the Ishani et al., 2015 study was based on the US Renal Data system that may not align with the Australian population. Additionally this observational study could not evaluate the effect of parathyroidectomy on risk of mortality because of the study design.
- 6.9 As a minor submission, these retrospective observational studies were not evaluated.

### ***Clinical claim***

- 6.10 The submission claimed that Pharmacor Cinacalcet provides equivalent effectiveness and safety to the previously listed brand, Sensipar. The PBAC noted that TGA considered the two brands to be bioequivalent.
- 6.11 Therefore, based on the bioequivalence statement, the PBAC considered that the claims of non-inferior comparative effectiveness and safety were reasonable.

### ***Economic analysis***

- 6.12 No economic analysis was presented in the submission as this was a minor submission.
- 6.13 The submission noted that it had no knowledge of the effective PBS price for Sensipar prior to it being delisted in August 2015 given the SPA that was applied. Therefore, the

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submission used the last published AEMP for Sensipar (July 2015) and derived from these the current DPMQ using April 2019 mark-ups and fees.

6.14 The submission noted at the March 2014 meeting, the PBAC considered that a significant price reduction to Sensipar would be needed to restore the cost-effectiveness of Sensipar to the level considered to be acceptable in 2007. The sponsor indicated in the Pre-PBAC response that a request for an SPA would be unlikely.

6.15 Table 1 summarises the proposed published prices presented in the submission.

**Table 1: Last published AEMP for Sensipar and published prices proposed for Pharmacor Cinacalcet**

Cinacalcet hydrochloride, Oral tablets		Max quantity	No. of Rpts	AEMP	DPMQ	
				July 2015	July 2015	April 2019
General Pharmaceutical Benefits						
9157Y	30 mg, 28 tablets	1	5	\$192.96	\$217.89	\$ [REDACTED]
9158B	60 mg, 28 tablets	1	5	\$385.92	\$425.36	\$ [REDACTED]
9159C	90 mg, 28 tablets	1	5	\$578.88	\$632.83	\$ [REDACTED]
Highly Specialised Drugs (Private Hospital)^						
9625N	30 mg, 28 tablets	2	5	\$192.96	\$408.29	\$ [REDACTED]
9626P	60 mg, 28 tablets	2	5	\$385.92	\$809.65	\$ [REDACTED]
9627Q	90 mg, 28 tablets	2	5	\$578.88	\$1,204.69	\$ [REDACTED]
Highly Specialised Drugs (Public Hospital)*						
5621W	30 mg, 28 tablets	2	5	\$192.96	\$385.92	\$ [REDACTED]
5622X	60 mg, 28 tablets	2	5	\$385.92	\$771.84	\$ [REDACTED]
5623Y	90 mg, 28 tablets	2	5	\$578.88	\$1,157.76	\$ [REDACTED]

\* Public Hospital DPMQ = AEMP x 2

^ Private Hospital DPMQ = (AEMP x 2) + \$7.92 dispense fee + 4% mark-up for ex.man between \$100.01 and \$1000 and \$40 for ex.man greater than \$1000

Note: the submission (p20) noted there was a 35% price reduction in the public price of Sensipar in September 2014.

Source: Excel Financials, 3b. proposed published prices; and Table 5, pg.21 of submission.

6.16 While not a matter for the PBAC to consider, the PBAC also noted the highest possible price should cinacalcet still be currently listed, incorporating anniversary price reductions as per sections 99ACHA and 99ACJ of the *National Health Act 1953*. The pre-PBAC response did not agree to the retrospective application of F1 anniversary price reductions to a product that was not listed at the time of anniversary reductions. The PBAC considered this to be a matter between the Sponsor and the Department.

**Drug cost/patient/year: \$ [REDACTED] (30 mg dose) - \$ [REDACTED] (180 mg dose)**

6.17 The submission did not estimate the drug cost/patient/year. There is a low level of certainty around the daily dosing for cinacalcet as the dose is variable and can be titrated up to a maximum dose of 180 mg. The submission presented the following average daily doses from various sources:

- EVOLVE ITT: 66.8 mg daily; with multivariate adjusted dose of 39.63 mg daily;
- PBS data (August 2013 – July 2015): 35 mg – 46 mg daily; assuming most patients took 1 tablet per day of the strength dispensed. Average daily dose of all Sensipar listings: 46 mg daily;

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- Alternative daily dosing regimens suggested in the cinacalcet November 2013 PSD: 52.1 mg (Adelaide utilisation data); 62.1 mg (Tasmanian data);
- Observation study presented in submission (Ruderman et al., 2019): 30 mg daily
- Average of all sources presented in submission: 35 mg – 40 mg daily.

6.18 The cycle length for cinacalcet can also be variable. The median duration of treatment in the EVOLVE trial was 21.2 months. It is likely that treatment with cinacalcet for SHPT would be chronic.

6.19 Given the variability of the dosing and treatment duration of cinacalcet treatment, based on the lowest and highest allowable dose of cinacalcet over a 12 month period; and using the prices under the General Schedule as this is the most likely setting for maintenance therapy, the range for drug cost/patient/year for cinacalcet is:

- 30 mg dose: 30 mg tablets (proposed published DPMQ) \$ [REDACTED] x 12 months = \$ [REDACTED]
- 180 mg dose: 90 mg tablets (proposed published DPMQ) \$ [REDACTED] (max qty of 2) x 12 months = \$ [REDACTED]

This calculation does not account for dose titration and wastage, or the effective price of cinacalcet.

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

6.20 The submission used a market share approach to estimate the likely financial implications of the proposed listing. The submission used MBS/PBS item reports between August 2013 and July 2015 for cinacalcet and projected the observed linear rate of growth to the current forecast period. The last published AEMP and sponsor-derived DPMQs were applied and past concessional splits were utilised to estimate the expected cost to government. It is noted that cinacalcet was listed from 1 July 2008 to 31 July 2015, however only 24 months of listing data were included in the estimates. The submission also derived one linear equation to estimate the financial projections (which resulted in an increase in the number of cinacalcet scripts of 6% to 8% per year).

6.21 The submission did not expect there to be any change in the number of MBS services as the patients in the proposed population are in constant contact with prescribers.

6.22 Table 2 presents the submission's estimated use and financial implications for cinacalcet. The net cost of cinacalcet to PBS/RPBS was incorrectly calculated in the submission where the patient co-payments were added to the PBS/RPBS costs, rather than being subtracted from the PBS/RPBS costs. This has been corrected in the table below. As these costs were based on the published price of Sensipar, the net cost to the PBS will reduce once the effective price of Sensipar is applied.

**Table 2: Estimated use and financial implications**

	Year 1 2019	Year 2 2020	Year 3 2021	Year 4 2022	Year 5 2023	Year 6 2024
<b>Estimated extent of use</b>						
Total number of scripts dispensed <sup>a</sup>						
<b>Estimated financial implications of Pharmacor Cinacalcet</b>						
Cost to PBS	\$	\$	\$	\$	\$	\$
Cost to RPBS	\$	\$	\$	\$	\$	\$
Cost to PBS/RPBS	\$	\$	\$	\$	\$	\$
Copayments	-\$	-\$	-\$	-\$	-\$	-\$
Cost to PBS/RPBS less copayments	\$	\$	\$	\$	\$	\$
<b>Net financial implications</b>						
Net cost to PBS/RPBS	\$	\$	\$	\$	\$	\$
Less cost to Hospitals <sup>^</sup>	-\$	-\$	-\$	-\$	-\$	-\$
Net cost to Government	\$	\$	\$	\$	\$	\$

<sup>a</sup> The submission estimated the script numbers using a linear equation to predict expected demand based on script numbers over a 24 month period when it was last listed (Aug 2013 – July 2015). It includes forecasted script numbers for all strengths.

<sup>^</sup> Estimated potential savings due to avoiding parathyroidectomy surgery assuming % of 2,500 patients who were using cinacalcet prior to its de-listing will avoid a parathyroidectomy. The cost per parathyroidectomy was based on the National Efficient Price Determination 2018-19, in which costs for parathyroid procedures were \$6,709 to \$12,539 based on ‘minor’ and ‘major’ complexities respectively.

Source: 3b. proposed published prices worksheet of Excel Financials spreadsheet; Table 7, p26 of the submission.

Note: values in italics were corrected by the Department. The net cost of cinacalcet to PBS/RPBS was incorrectly calculated in the submission where the patient co-payments were added to the PBS/RPBS costs, rather than being subtracted from the PBS/RPBS costs.

The redacted table shows that at Year 6, the net cost to the PBS would be \$20 - \$30 million.

6.23 The submission claimed that re-listing cinacalcet will likely result in a reduction in parathyroidectomy surgery. The submission estimated that this would result in a potential saving of less than \$10 million per year. The submission included the potential savings from avoiding parathyroidectomy surgery in the financial estimates to calculate the net cost to Government. However, the estimated savings associated with the surgeries that were presented in the submission would not form part of the costs to the PBS or MBS, and therefore did not affect the financial estimates for the Commonwealth, as these are costs to Public Hospital system.

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

## 7 PBAC Outcome

7.1 The PBAC recommended the listing of cinacalcet for the treatment of secondary hyperparathyroidism (SHPT) in patients with chronic kidney disease (CKD) receiving dialysis, on the basis that it should be available only through special arrangements under the Section 100 Highly Specialised Drugs Program for initial and continuing treatment and the Section 85 General Schedule for continuing treatment.

7.2 The PBAC’s recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of cinacalcet would be acceptable if it were

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priced equivalent to the lowest effective price of Sensipar before delisting on 1 August 2015.

- 7.3 The PBAC was satisfied that cinacalcet meets a moderate unmet clinical need in the target population since there is currently no specific alternative calcimimetic available on the PBS for patients with CKD receiving dialysis with SHPT. The PBAC considered that the claim that there has been an increase in parathyroidectomy surgery rates due to the unavailability of cinacalcet was likely to be reasonable.
- 7.4 The PBAC noted that Pharmacor Cinacalcet was found to be bioequivalent to Sensipar by the TGA.
- 7.5 The submission did not nominate a comparator, however the PBAC noted that the listing and pricing arrangement for cinacalcet was proposed in the submission to be consistent with the previous listing for Sensipar.
- 7.6 The PBAC considered the request to list under Section 100 (Highly Specialised Drugs Program) Public and Private Hospital was appropriate for the initiation listing. The PBAC considered that a nephrologist would be the appropriate prescriber to initiate treatment with cinacalcet as patients would be on dialysis within the hospital setting.
- 7.7 The PBAC also recommended the Section 85 General Schedule listing for continuing therapy to allow medical or nurse practitioners to prescribe cinacalcet. The PBAC considered that this would assist continuity of care and allow for more equitable access to cinacalcet.
- 7.8 The PBAC advised the following for the listing of cinacalcet:
- initial therapy should be Authority Required (Telephone) and continuing therapy should be Authority Required (Streamlined);
  - the requested maximum quantity and repeats were appropriate; and
  - the proposed restriction should align with the previous listing of Sensipar and current KDIGO guidelines.
- 7.9 The PBAC noted that the EVOLVE study was underpowered to detect a difference in younger patients and maintained its views from previous considerations that although age appears to be a treatment-effect modifier, the PBAC did not consider it was plausible that a patient would derive such a marked variation in clinical benefit as proposed in the submission, only on the basis of being aged under or over 65 years.
- 7.10 The PBAC considered that the data from the EVOLVE trial presented in the submission did not provide conclusive evidence that cinacalcet improved clinical outcomes for patients, such as reducing the risk of death or major cardiovascular events. The PBAC re-affirmed its view that the EVOLVE trial did not demonstrate a statistically significant difference over placebo in the primary outcome, and there was a higher incidence of adverse events with cinacalcet. Further, the PBAC noted that the observational data provided in the submission did not provide conclusive evidence that cinacalcet

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improved clinical outcomes for patients such as reducing the risk of death or major cardiovascular events.

- 7.11 In terms of the clinical claim, the PBAC considered that given the TGA considered the two brands of cinacalcet (Pharmacor Cinacalcet and Sensipar) to be bioequivalent, the PBAC accepted that Pharmacor Cinacalcet was non-inferior in terms of comparative effectiveness and safety to Sensipar.
- 7.12 The PBAC accepted that the listing of cinacalcet will result in a cost to the PBS, but as the financial estimates presented in the submission were based on the published price of Sensipar, the net cost to the PBS will reduce once the effective price of Sensipar is applied.
- 7.13 The PBAC recommended that the Early Supply Rule should not apply as the dosing for cinacalcet may be variable. This was consistent with the Committee's recommendation for Sensipar at its November 2007 meeting.
- 7.14 The PBAC recommended that cinacalcet is suitable for inclusion in the PBS medicines for prescribing by nurse practitioners in the continuing treatment phase of the Section 85 General listing. This was consistent with the Committee's recommendation for Sensipar at its November 2007 meeting.
- 7.15 The PBAC also recommended that under Section 101(3BA) of the *National Health Act 1953* cinacalcet should not be treated as interchangeable with any other drugs or medicinal preparations on an individual patient basis.
- 7.16 The PBAC noted that its recommendation was for the listing of a new brand of cinacalcet under the same circumstances as a previously listed cinacalcet brand, which was delisted by the relevant sponsor in August 2015. The PBAC advised that the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009* for Pricing Pathway A were not met because the efficacy and toxicity of cinacalcet were unchanged, and while the PBAC was satisfied that the re-listing of cinacalcet would meet a moderate unmet clinical need (paragraph 7.3) that need was not high or urgent.
- 7.17 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 item:

#### Listing 1. HSD Private/Public Hospital – Initiation

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
CINACALCET HYDROCHLORIDE				
Tablet, 30 mg, 28	2	5		
Tablet, 60 mg, 28	2	5	Pharmacor Cinacalcet Tablets	Pharmacor Pty Ltd
Tablet, 90 mg, 28	2	5		

<b>Category / Program:</b>	Section 100 – Highly Specialised Drugs Program (Private Hospital) Section 100 – Highly Specialised Drugs Program (Public Hospital)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Condition:</b>	Secondary hyperparathyroidism
<b>PBS Indication:</b>	Secondary hyperparathyroidism
<b>Treatment phase:</b>	Initial
<b>Restriction Level / Method:</b>	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required – In Writing <input checked="" type="checkbox"/> Authority Required – Telephone/Electronic/Emergency <input type="checkbox"/> Streamlined
<b>Treatment criteria:</b>	Must be treated by a nephrologist
<b>Clinical criteria:</b>	The patient must have chronic kidney disease <b>AND</b> The patient must be on dialysis <b>AND</b> The patient must not have responded to conventional therapy <b>AND</b> The patient must have sustained hyperparathyroidism with iPTH of at least 50 pmol per L <b>OR</b> The patient must have sustained hyperparathyroidism with iPTH of at least 15 pmol per L and less than 50 pmol per L AND an (adjusted) serum calcium concentration at least 2.6 mmol per L
<b>Prescriber Instructions:</b>	During the titration phase, intact PTH should be monitored 4 weekly (measured at least 12 hours post dose) and dose titrated until an appropriate iPTH concentration is achieved. During the titration phase, prescribers should request approval to allow sufficient supply for 4 weeks treatment at a time, with doses between 30 and 180 mg per day according to the patient's response and tolerability.
<b>Administrative Advice:</b>	"Sustained" means the abnormality was detected on at least 2 blood samples collected over a period of 2 to 4 months.

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**Listing 2. HSD Private/Public Hospital – Continuation**

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
CINACALCET HYDROCHLORIDE				
Tablet, 30 mg, 28	2	5		
Tablet, 60 mg, 28	2	5	Pharmacor Cinacalcet Tablets	Pharmacor Pty Ltd
Tablet, 90 mg, 28	2	5		

<b>Category / Program:</b>	Section 100 – Highly Specialised Drugs Program (Private Hospital) Section 100 – Highly Specialised Drugs Program (Public Hospital)
<b>Prescriber type:</b>	<input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
<b>Condition:</b>	Secondary hyperparathyroidism
<b>PBS Indication:</b>	Secondary hyperparathyroidism
<b>Treatment phase:</b>	Continuing
<b>Restriction Level / Method:</b>	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required – In Writing <input type="checkbox"/> Authority Required – Telephone/Electronic/Emergency <input checked="" type="checkbox"/> Streamlined
<b>Treatment criteria:</b>	Must be treated by a nephrologist
<b>Clinical criteria:</b>	The patient must have chronic kidney disease <b>AND</b> The patient must be on dialysis <b>AND</b> The patient must have previously received PBS-subsidised treatment with this drug for this condition
<b>Prescriber Instructions:</b>	During the maintenance phase, prescribers should request approval to allow sufficient supply for 4 weeks treatment up to a maximum of 6 months supply, with doses between 30 and 180 mg per day according to the patient's response and tolerability. Intact PTH should be monitored quarterly (measured at least 12 hours post dose) and dose adjusted as necessary to maintain an appropriate iPTH concentration.
<b>Administrative Advice:</b>	"Sustained" means the abnormality was detected on at least 2 blood samples collected over a period of 2 to 4 months.

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**Listing 3. General Schedule – Continuation only**

Name, Restriction, Manner of administration and form	Max. Qty	No. of Rpts	Proprietary Name and Manufacturer	
CINACALCET HYDROCHLORIDE				
Tablet, 30 mg, 28	1	5		
Tablet, 60 mg, 28	1	5	Pharmacor Cinacalcet Tablets	Pharmacor Pty Ltd
Tablet, 90 mg, 28	1	5		

<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>	Secondary hyperparathyroidism
<b>PBS Indication:</b>	Secondary hyperparathyroidism
<b>Treatment phase:</b>	Continuing
<b>Restriction Level / Method:</b>	<input type="checkbox"/> Restricted benefit <input type="checkbox"/> Authority Required – In Writing <input type="checkbox"/> Authority Required – Telephone/Electronic/Emergency <input checked="" type="checkbox"/> Streamlined
<b>Clinical criteria:</b>	The patient must have chronic kidney disease <b>AND</b> The patient must be on dialysis <b>AND</b> The patient must have had a decrease of at least 30% in iPTH concentrations after 6 months treatment <b>OR</b> The patient must have had iPTH greater than 15 pmol per L and an (adjusted) serum calcium concentration of less than 2.6 mmol per L after 6 months treatment
<b>Prescriber Instructions:</b>	During the maintenance phase, prescribers should request approval to allow sufficient supply for 4 weeks treatment up to a maximum of 6 months supply, with doses between 30 and 180 mg per day according to the patient's response and tolerability. Intact PTH should be monitored quarterly (measured at least 12 hours post dose) and dose adjusted as necessary to maintain an appropriate iPTH concentration.
<b>Administrative Advice:</b>	Continuing Therapy Only: 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.

## 9 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.

## **10 Sponsor's Comment**

The sponsor thanks the PBAC for its deliberations and looks forward to working with the Department to return cinacalcet to the PBS.