National PBM Drug Monograph
Cinacalcet HCl (Sensipar™)

VA Pharmacy Benefits Management Strategic Health Care Group and the Medical Advisory Panel

Executive Summary

- **Indications:** Cinacalcet HCl (Sensipar™) is a calcimimetic agent, approved by the FDA for the treatment of secondary hyperparathyroidism (HPT) in patients with chronic kidney disease on dialysis and for the treatment of hypercalcemia in patients with parathyroid carcinoma.

- **Efficacy:** Cinacalcet has been shown to decrease PTH levels by approximately 43% (statistically significant compared to baseline and compared to placebo) in patients with secondary HPT on chronic hemodialysis (ARR 38%, NNT=3 patients to achieve PTH $\leq$ 250 pg/ml with 14 weeks treatment). There was also a statistically significant decrease in serum calcium, phosphorus, and calcium-phosphorus product (Ca X P) with cinacalcet compared to placebo.

- **Safety:** The most common adverse events associated with cinacalcet include nausea (31% vs. 19% on placebo) and vomiting (27% vs. 15% on placebo). As cinacalcet lowers serum calcium, patients should be monitored for hypocalcemia and it is recommended that cinacalcet not be started in patients with serum calcium less than the lower limit of normal (e.g., 8.4mg/dl). Cinacalcet is metabolized by the cytochrome P450 enzymes: primarily CYP3A4, CYP2D6, and CYP1A2. Upon initiation of a strong inhibitor of CYP3A4 (e.g., ketoconazole, erythromycin, itraconazole), dose adjustments of cinacalcet may be required and the PTH and serum calcium levels should be monitored closely. Cinacalcet is also a strong inhibitor of CYP2D6. Medications that are metabolized by CYP2D6 and that have a narrow therapeutic index (e.g., flecainide, vinblastine, thioridazine and most tricyclic antidepressants) may require dose adjustment. Seizures were reported in 1.4% of patients receiving cinacalcet compared to 0.4% patients on placebo. Although the mechanism for the difference in incidence has not been established, it is recommended that serum calcium levels be closely monitored in patients receiving cinacalcet, especially those with a history of seizure disorder, as a significant reduction in serum calcium may lower the seizure threshold.

- **Laboratory monitoring:** Secondary HPT: monitor serum calcium and phosphorus within 1 week and intact PTH within 1 to 4 weeks of initiation or change in therapy; monitor calcium and phosphorus every month and intact PTH every 1 to 3 months while on maintenance therapy. Parathyroid carcinoma: monitor serum calcium within 1 week of initiation or change in therapy and every 2 months while on maintenance therapy.

- **Dose:** The initial recommended dose for patients with secondary HPT on hemodialysis is 30mg qd, with increases of 30mg qd increments no more frequently than every 2 to 4 weeks to 180mg qd based on target intact PTH. The initial recommended dose for patients with hypercalcemia due to parathyroid carcinoma is 30mg bid, with increases to a maximum of 90mg qid based on normalization of serum calcium. Cinacalcet should be taken whole and not divided. The dose should be taken with food or soon after a meal.

- **Cost:** The annual drug cost of treatment with cinacalcet for patients with secondary HPT and chronic kidney disease on dialysis is $2,000 to $13,000, depending on the dose. For the treatment of hypercalcemia in patients with parathyroid carcinoma, the annual drug cost of treatment with cinacalcet is $4,300 to $25,800, depending on the dose.

- **Recommendations:** It is recommended that cinacalcet be available for nonformulary use according to well-defined criteria that will be developed with input from formulary managers and subject matter experts.

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Introduction[1-9]

Cinacalcet HCl (Sensipar™ Amgen) received FDA approval for marketing in the U.S. on March 8, 2004. Cinacalcet is the first calcimimetic agent to be approved for the treatment of secondary hyperparathyroidism (HPT) in patients with chronic kidney disease (CKD) on dialysis and for the treatment of hypercalcemia in patients with parathyroid carcinoma.[1]

Patients with CKD often have an increase in parathyroid hormone (PTH) that is thought to be secondary to a reduced serum calcium due to a decrease in 1,25-dihydroxyvitamin D_3 (1,25-$(OH)_2$ D_3) and increased serum phosphorus.[2] Secondary HPT is reported to be common in patients with CKD although the exact prevalence is not known. An evaluation at two hemodialysis centers found an elevated intact PTH (iPTH) level of > 200pg/ml in 78% of patients on chronic hemodialysis.[3] Secondary HPT may lead to metabolic bone disease, with osteitis fibrosa seen in patients with iPTH levels over 400 pg/ml, although high-turnover bone lesions may also occur at lower levels.[4]

Current recommendations to reduce PTH include restriction of dietary phosphate or the use of vitamin D (e.g., calcitriol) in patients with an inadequate response or with levels > 300 pg/ml.[4] Calcium-based phosphate binders to reduce serum phosphorus[5] and increase serum calcium may result in hypercalcemia, which may contribute to an increase in the calcium-phosphate product (Ca X P) that has been related to an increase in mortality[6] and mortality due to coronary artery disease and sudden death[7] in patients on chronic hemodialysis. Non-ionic phosphate binders are also available to reduce serum phosphorus in selected circumstances (refer to the Criteria for Nonformulary Use of Sevelamer HCl in VA Patients with CKD and Kidney Failure on Dialysis at http://www.vapbm.org/criteria/Sevelamecriteria.pdf). Treatment with vitamin D may also be accompanied by an increase in serum calcium and phosphorus.[5]

The calcimimetics are a new class of agents that decrease secretion of PTH without resulting in increased calcium or phosphorus levels although the long-term effects of reducing PTH to target levels are unknown.[8] In addition, calcimimetics may reduce the development of parathyroid gland hyperplasia.[9]

Pharmacology[1,2,4]

In CKD, phosphorus retention results in a reduction in 1,25-$(OH)_2$ D_3 and serum calcium that leads to an increase in PTH (secondary HPT). In kidney disease, there is a persistent increase in PTH, in an attempt to regulate the levels of phosphorus and calcium through the effect of 1,25-$(OH)_2$ D_3 on bone, resulting in high-turnover bone disease (e.g., osteitis fibrosa). As discussed above, current treatments act to either reduce serum phosphorus (dietary restriction, phosphate binders) or increase serum calcium (vitamin D), which can result in an increase in the Ca X P.[2,4]

Cinacalcet is a calcimimetic agent that acts at the calcium-sensing receptor in the parathyroid gland, increasing the sensitivity of these receptors to serum calcium. This action results in a reduction in PTH secretion that is accompanied by a reduction in serum calcium.[1]

Pharmacokinetics[1]

C_{max}	Vd	Protein binding	t½	Metabolism	Excretion	Food effect
2-6 hrs	1000 L	93-97%	30-40 hrs	CYP3A4 CYP2D6 CYP1A2	80% urine 15% feces	High-fat meal: C_{max} ↑ 82%; AUC ↑ 68% Low-fat meal: C_{max} ↑ 65%; AUC ↑ 50%

FDA Approved Indication(s) and Off-Label Uses[1]

Cinacalcet HCl is approved for the treatment of secondary hyperparathyroidism in patients with chronic kidney disease on dialysis and for the treatment of hypercalcemia in patients with parathyroid carcinoma.

The use of cinacalcet as primary therapy in patients with secondary HPT, in patients not on chronic hemodialysis, or in patients with primary HPT has not been adequately studied.

Dosage and Administration[1]

General Recommendations: Cinacalcet should be taken whole and not divided. The dose should be taken with food or soon after a meal.

Recommendations for patients with secondary HPT and CKD on dialysis: Cinacalcet may be used alone or in combination with vitamin D sterols with or without phosphate binders.

Starting Dose	Lab Monitoring for Dose Adjustment	Target iPTH	Titration Interval	Sequential Dose Titration
30mg qd	1-4 wks: iPTH 1 wk: serum calcium and phosphorus*	150-300pg/mL	q 2-4 wks	60mg qd, 90mg qd, 120mg qd, 180mg qd

*If calcium levels decrease below normal range, attempts should be made to return calcium levels to normal (e.g., supplemental calcium, initiating or increasing calcium-based phosphate binders, initiating or increasing vitamin D, or temporarily holding treatment with cinacalcet)

Recommendations for patients with parathyroid carcinoma:

Starting Dose	Lab Monitoring for Dose Adjustment	Target Calcium	Titration Interval	Sequential Dose Titration
30mg bid	Within 1 wk: serum calcium	Normal range for lab	q 2-4 wks	30mg bid, 60mg bid, 90mg bid, 90mg tid, 90mg qid

Adverse Events[1]

The most frequently reported adverse events in patients with secondary HPT and CKD on dialysis or patients with parathyroid carcinoma were nausea and vomiting.

Adverse Event*	% Placebo (n=470)	% Cinacalcet (n=656)
Nausea	19	31
Vomiting	15	27
Diarrhea	20	21
Myalgia	14	15
Dizziness	8	10
Hypertension	5	7
Asthenia	4	7
Anorexia	4	6
Chest pain, noncardiac	4	6
Access infection	4	5

*Adverse events reported in $\geq$ 5% of patients on dialysis and at a greater percentage in patients on cinacalcet vs. placebo

Long-term safety: A double blind-extension study of 6 months (12 months total treatment) in 266 patients with secondary HPT and CKD on dialysis reported a similar incidence of adverse events in the two treatment groups that were also similar to previous trials.

Look-alike/Sound-alike Error Risk Potential

As part of a pilot program, the VA PBM and Center for Medication Safety queried a multi-attribute drug product search engine for similar sounding and appearing drug names based on orthographic and phonological similarities, as well as similarities in dosage form, strength and route of administration. By incorporating similarity scores as well as clinical judgment, it was determined that the following drug names may pose as potential sources of drug name confusion.

Cinacalcet (generic name)
Potential name confusion: Calcet (calcium/vitamin D combination product)
Potential Severity: Minor-Moderate (depending on the patient's calcium)
Probability: Occasional

Sensipar (brand name)
Potential name confusion: Buspar, Senna products
Potential Severity: Minor for both
Probability: Remote

Contraindications[1]

Cinacalcet is contraindicated in patients with a known hypersensitivity to the drug or its components.

Warnings[1]

Seizures: Seizures, primarily generalized or tonic-clonic, were reported in 1.4% of patients receiving cinacalcet (9/656) compared to 0.4% patients on placebo (2/470). Seizures occurred in 5 of the 9 cinacalcet patients (with 2 receiving anti-seizure medication) and in the 2 patients on placebo who had a history of seizure disorder and were on anti-seizure medications. Although the mechanism for the difference in incidence has not been established, it is recommended that serum calcium levels be closely monitored in patients receiving cinacalcet, especially those with a history of seizure disorder, as a significant reduction in serum calcium may lower the seizure threshold.

Precautions[1]

Hypocalcemia: As cinacalcet lowers serum calcium, patients should be monitored for hypocalcemia (refer to recommendations in section on Laboratory Monitoring below). It is recommended that cinacalcet not be started in patients with serum calcium less than the lower limit of normal (e.g., 8.4mg/dl). Once initiated, if serum calcium falls to 7.6-8.3mg/dl, or if the patient exhibits symptoms of hypocalcemia (e.g., paresthesias, myalgias, cramping, tetany, or convulsions), a calcium-based phosphate binder and/or vitamin D sterols can be used to increase serum calcium. If the serum calcium is < 7.5mg/dl or if symptoms of hypocalcemia continue and the vitamin D dose cannot be increased, cinacalcet should be withheld until the serum calcium is $\geq$ 8.0mg/dl or symptoms of hypocalcemia resolve. Cinacalcet can then be restarted at the next lowest dose.

Adynamic Bone Disease: If iPTH levels are below 100pg/ml, adynamic bone disease may develop. It is recommended that the dose of cinacalcet and/or vitamin D sterols should be reduced or discontinued if iPTH levels decrease below 150-300 pg/ml (target range per the National Kidney Foundation K/DOQI guidelines).[4]

Hepatic Insufficiency: In patients with moderate to severe hepatic impairment, the AUC of cinacalcet was 2.4 and 4.2 times higher, respectively compared to normal individuals. The mean t ½ is prolonged by 33% in patients with moderate hepatic impairment and by 70% in those with severe impairment. It is recommended that PTH and serum calcium be closely monitored in patients with moderate to severe hepatic impairment.

Pregnancy Category C: There have not been any adequate well-controlled studies in pregnant women. Studies in rats have shown that at a dose 2-3 times the human dose there was evidence of maternal signs of hypocalcemia and a decrease in postnatal maternal and pup body weight gain. Reductions in maternal food consumption and body weight gain were seen in pregnant female rabbits exposed to less than a human oral dose of cinacalcet. Cinacalcet should only be used in pregnant females if the potential benefit outweighs the potential risk to the fetus.

Nursing Mothers: It is not known whether the drug is excreted in human milk. Cinacalcet is excreted in the milk with a high milk-to-plasma ratio in studies in rats. Due to the potential for a clinically significant adverse effect, it is recommended that a decision be made to either discontinue nursing or discontinue the drug, taking into consideration the potential benefit to the patient.

Special Patient Populations[1]

Demographics (Age): Patients 65 years of age or older have a similar pharmacokinetic profile compared to patients less than 65 years of age. The pharmacokinetics of cinacalcet have not been studied in patients less than 18 years of age. The safety and efficacy of cinacalcet have not been established in pediatric patients.

Laboratory Monitoring[1]

	Serum calcium	Serum phosphorus	iPTH*
Secondary HPT and CKD on dialysis			
After initiation/dose adjustment	Within 1 week	Within 1 week	1 to 4 weeks
On maintenance dose	Monthly	Monthly	Every 1-3 months
Parathyroid carcinoma			
After initiation/dose adjustment	Within 1 week		
On maintenance dose	Every 2 months		

* The Nichols IRMA was used to obtain all iPTH measurements during the clinical trials

Drug Interactions[1]

Effects of other medications on cinacalcet:

- Cinacalcet is metabolized by the cytochrome P450 enzymes, primarily CYP3A4, CYP2D6, and CYP1A2.
- Upon initiation of a strong inhibitor of CYP3A4 (e.g., ketoconazole, erythromycin, itraconazole), dose adjustments of cinacalcet may be required and the PTH and serum calcium levels should be monitored closely.
- Ketoconazole (strong inhibitor of CYP3A4): Concomitant administration of ketoconazole 200mg bid increased cinacalcet AUC and Cmax by 2.2 and 2.3 times, respectively after a single 90mg dose of cinacalcet.

Effects of cinacalcet on other medications:

- Cinacalcet is a strong inhibitor of CYP2D6 (but not CYP1A2, CYP2C9, CYP2C19, or CYP3A4) according to in vitro studies.
- Medications that are metabolized by CYP2D6 and that have a narrow therapeutic index [e.g., flecainide, vinblastine, thioridazine and most tricyclic antidepressants (e.g., amitriptyline, clomipramine, desipramine, doxepin, imipramine, maprotiline, nortriptyline)] may require dose adjustment.
- Amitriptyline: Concomitant administration of 50mg with cinacalcet 25mg or 100mg increased amitriptyline exposure and nortriptyline (active metabolite) approximately 20% in extensive metabolizers of CYP2D6.

Efficacy Measures[10]

The long-term effects (skeletal or cardiovascular) of cinacalcet on lowering PTH levels have not been published (other than in abstract from). The efficacy measures in the randomized, placebo-controlled trials presented below include:

Secondary HPT and CKD on dialysis:

Primary endpoint
- mean PTH level ≤ 250 pg/ml

Secondary endpoints
- decrease of ≥ 30% mean PTH level vs. baseline
- % change PTH level
- % change calcium, phosphorus, and Ca X P

Parathyroid carcinoma: serum calcium

Clinical Trial Data[10-14]

Secondary HPT and CKD on dialysis: Five publications of randomized, placebo-controlled trials were identified in patients with secondary HPT:[10-14] one combining results of two randomized, controlled trials (presented below);[10] one dose-finding study;[11] two dose titration studies;[12,13] and one single-dose and 8-day multiple-dose phase.[14]

<table>
<tr><th>Trial</th><th>Inclusion/Exclusion/Endpoints</th><th>Treatment</th><th>Results</th><th>Adverse Events/Withdrawals</th></tr>
<tr>
<td>Block et al, 2004[10]

Two R, DB, PC, MC trials of identical design (63 sites North America; 62 sites Europe and Australia)</td>
<td><u>Inclusion criteria</u>
≥ 18 yrs of age, secondary HPT, mean PTH level > 300 pg/ml, HD 3 times/wk ≥ 3 months, medically stable

<u>Exclusion criteria</u>
Cancer, active infection, disease that causes hypercalcemia, serum Ca < 8.4mg/dl (corrected for albumin); concomitant flecainide, thioridazine, most TCAs, that have a NTI and metabolized by CYP 2D6; no more than 20% could have PTH level > 800 pg/ml

1270 screened/741 eligible/741 enrolled

Randomization stratified by disease severity, baseline Ca X P

<u>Endpoints</u>
Primary: proportion with mean PTH level ≤ 250 pg/ml during efficacy-assessment phase

Secondary: proportion with ↓ of ≥ 30% mean PTH level vs. baseline; % change in PTH level, Ca, phosphorus, and Ca X P</td>
<td><u>26 wks duration</u>
(cinacalcet vs. placebo)

Dose titration (12 wks): 30mg qd, ↑'d q3wks to 60mg, 90mg, 120mg, 180mg qd if PTH > 200 pg/ml and serum Ca ≥ 7.8 mg/dL (no ↑ if symptoms of hypocalcemia, serum Ca < 7.8 mg/dl or AE where dose should not be↑'d; dose ↓'d if PTH levels < 100 pg/ml X 3 or AE requiring ↓ dose)

Efficacy-assessment (14 wks): Dose adjustments permitted q4wks

Concomitant therapy (standard of care): phosphate-binders (no restrictions on dose or type) and/or vitamin D sterols allowed (dose ↑ if PTH level ↑'d ≥ 50% baseline, if serum Ca < 8.4 mg/dl, or if symptoms of hypocalcemia; dose ↓ if serum Ca ≥ 11 mg/dl, phosphorus ≥ 6.5 mg/dl, Ca X P ≥ 70 mg^2/dl^2, or PTH level < 100 pg/ml X 3 on lowest cinacalcet dose)

Dialysate Ca levels unchanged</td>
<td>Baseline (mean): age 54-55yrs; 61-62% male; 56-61% white; duration HD 72 months; 66-67% vitamin D sterols; 92-93% phosphate binders (40-44% Ca-based only, 24-25% sevelamer only)
<table>
<tr><th>Endpoint</th><th>Cinacalcet (N=371)</th><th>Placebo (N=370)</th><th>P value</th></tr>
<tr><td>Primary</td><td>160 (43%)</td><td>19 (5%)</td><td><0.001</td></tr>
<tr><td>Secondary</td><td>239 (64%)</td><td>42 (11%)</td><td><0.001</td></tr>
<tr><td>PTH (pg/ml)</td><td></td><td></td><td></td></tr>
<tr><td>Baseline</td><td>643±18</td><td>642±19</td><td></td></tr>
<tr><td>EA</td><td>374±19**</td><td>693±23</td><td><0.001</td></tr>
<tr><td>% change</td><td>-43±2</td><td>9±2</td><td><0.001</td></tr>
<tr><td>PTH* (pg/ml)</td><td></td><td></td><td></td></tr>
<tr><td>Baseline</td><td>326±14</td><td>337±16</td><td></td></tr>
<tr><td>EA</td><td>200±15**</td><td>396±18***</td><td><0.001</td></tr>
<tr><td>% change</td><td>-38±3</td><td>23±4</td><td><0.001</td></tr>
<tr><td>Ca (mg/dl)</td><td></td><td></td><td></td></tr>
<tr><td>Baseline</td><td>9.9±0</td><td>9.9±0</td><td></td></tr>
<tr><td>EA</td><td>9.2±0**</td><td>9.9±0</td><td><0.001</td></tr>
<tr><td>% change</td><td>-6.8±0.4</td><td>0.4±0.3</td><td><0.001</td></tr>
<tr><td>Phosphorus (mg/dl)</td><td></td><td></td><td></td></tr>
<tr><td>Baseline</td><td>6.2±0.1</td><td>6.2±0.1</td><td></td></tr>
<tr><td>EA</td><td>5.6±0.1**</td><td>6.0±0.1</td><td><0.001</td></tr>
<tr><td>% change</td><td>-8.4±1.3</td><td>0.2±1.3</td><td><0.001</td></tr>
<tr><td>Ca X P (mg^2/dl^2)</td><td></td><td></td><td></td></tr>
<tr><td>Baseline</td><td>62±0.8</td><td>61±0.8</td><td></td></tr>
<tr><td>EA</td><td>51±0.8</td><td>60±0.8</td><td><0.001</td></tr>
<tr><td>% change</td><td>-14.6±1.3</td><td>0.5±1.3</td><td><0.001</td></tr>
</table>
*Plasma full-length PTH (North American sites only: cinacalcet N=205; placebo N=205); **P<0.001 vs. baseline; ***P=0.01 vs. baseline
<u>Alkaline phosphatase</u>: cinacalcet ↓ 35% vs. placebo ↓ 4% (P<0.001)
<u>Vitamin D treatment (during study)</u>: cinacalcet 82% vs. placebo 78%
Cinacalcet reduced PTH levels by 52%, 43%, and 44% in patients whose vitamin D doses were ↑'d, ↓'d, or remained the same, respectively. Reductions in Ca X P with cinacalcet were 13%, 19%, and 17% in patients whose vitamin D doses were ↑'d, ↓'d, or remained the same, respectively.</td>
<td>Completed dose titration:
Cinacalcet (82%)
Placebo (88%)

Completed Efficacy-assessment:
Cinacalcet (68%)
Placebo (78%)

<table>
<tr><th>AE</th><th>Cinacalcet</th><th>Placebo</th></tr>
<tr><td>≥ 1 AE</td><td>91%</td><td>94%</td></tr>
<tr><td>W/D AE</td><td>15%</td><td>7%</td></tr>
<tr><td>Nausea</td><td>32%</td><td>19%*</td></tr>
<tr><td>Vomiting</td><td>30%</td><td>16%*</td></tr>
<tr><td>W/D N/V</td><td>5%</td><td>1%</td></tr>
<tr><td>Ca < 7.5</td><td>5%</td><td><1%*</td></tr>
<tr><td>W/D↓Ca</td><td>1 patient</td><td>1 patient</td></tr>
</table>
*P<0.001 vs. cinacalcet
Nausea: not dose-related
Vomiting: dose-related

Kidney transplant (withdrew):
Cinacalcet (4%)
Placebo (4%)

Death:
Cinacalcet (2%)
Placebo (2%)

Withdrew consent:
Cinacalcet (4%)
Placebo (3%)</td>
</tr>
</table>

Study Conclusions

- Cinacalcet decreased PTH levels by approximately 43% that was statistically significant compared to baseline and compared to placebo. There was also a statistically significant decrease in serum calcium, phosphorus and Ca X P with cinacalcet compared to placebo. The levels of PTH and Ca X P were reduced regardless of concomitant therapy with vitamin D.
- ARR of the primary endpoint (PTH level ≤ 250 pg/mL) was 38% with cinacalcet vs. placebo with a NNT of 3 patients to achieve the primary endpoint with 14 weeks treatment

Quality Assessment (Fair)

- Method of patient randomization and blinding of patient, investigator, or outcome assessor not reported
- No significant differences in baseline demographic characteristics
- Mean dose of cinacalcet not reported; dose adjustments of vitamin D sterols allowed
- High withdrawal rate
- Intention to treat analysis
- Involvement of sponsor (study design, central data-processing facility, statistical analysis and interpretation)

AE=adverse event; ARR=absolute risk reduction; Ca=calcium; Ca X P=calcium-phosphorus product; CYP=cytochrome P450; DB=double-blind; HD=hemodialysis; MC=multicenter; N=nausea; NNT=number needed to treat; NTI=narrow therapeutic index; PC=placebo-controlled; R=randomized; TCAs=tricyclic antidepressants; V=vomiting; W/D=withdrawal due to; wk=week; yrs=years

Parathyroid carcinoma: No published randomized controlled trials were identified. Approval for the treatment of hypercalcemia in patients with parathyroid carcinoma is based on an open-label study of 10 patients with parathyroid carcinoma (n=10, 2 to 16 week titration phase; n=3, 16 to 48 week maintenance phase). Baseline serum calcium was 14.7mg/dl with a range of change –7.4mg/dl to 2.7mg/dl during the titration phase and –7.4mg/dl to 0.9mg/dl during the maintenance phase (dose range 70mg bid to 90mg qid).[1]

Acquisition Cost

Drug	Dose	FSS Price/ Tablet	Drug Cost/ Patient/Month*	Annual Drug Cost/Patient*	Drug Cost/ Patient/Month**	Annual Drug Cost/Patient**
Cinacalcet	30mg	$5.9763	$179.29	$2151.47	$358.58	$4302.94
	60mg	$11.9527	$358.58	$4302.97	$717.16	$8605.94
	90mg	$17.9293	$537.88	$6454.55	$1075.76	$12909.10
	120mg (2 X 60mg)	($23.9054)	$717.162	$8605.94	NA	NA
	180mg (2 X 90mg)	($35.8586)	$1075.76	$12909.10	NA	NA
	90mg tid	($53.7879)	NA	NA	$1613.64	$19363.64
	90mg qid	($71.7172)	NA	NA	$2151.52	$25818.19

* Secondary HPT; qd dosing
** Parathyroid carcinoma; bid-qid dosing

Cost-Effectiveness Analysis

No cost-effectiveness data (in the literature or from the manufacturer) are available at this time.

Data Compilation Table

Primary Endpoint	Mean PTH ≤ 250 pg/ml
Results: Cinacalcet	160/371 (43%)
Results: Placebo	19/370 (5%)
Treatment duration	14 weeks
Relative Risk Reduction (95% CI)	20%
Absolute Risk Reduction (95% CI)	38% (32.49 to 43.52)
NNT (95% CI)	3 (2.30 to 3.08)

Conclusions

Cinacalcet has been reported to reduce PTH levels and Ca X P in patients with secondary HPT in a published, randomized, placebo-controlled trial. The majority of patients were also receiving therapy with phosphate-binders and vitamin D sterols. Although the benefit was seen in a subset of patients not receiving vitamin D sterols, further study is needed to recommend cinacalcet as primary therapy for secondary HPT. The long-term skeletal or cardiovascular effects of reducing PTH levels and/or Ca X P with cinacalcet is not available in published, randomized controlled trials.

Cinacalcet appears to be useful in reducing serum calcium in patients with hypercalcemia due to parathyroid carcinoma, although no published clinical trials are available.

Recommendations

It is recommended that cinacalcet be available for nonformulary use according to well-defined criteria that will be developed with input from formulary managers and subject matter experts.

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