HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use Sensipar safely and effectively. See full prescribing information for Sensipar.

Sensipar® (cinacalcet) Tablets
Initial US Approval: 2004

----------RECENT MAJOR CHANGES----------
Indications and Usage: Primary Hyperparathyroidism (1.3) 02/2011
Dosage and Administration: Parathyroid Carcinoma / Primary Hyperparathyroidism (2.2) 02/2011
Contraindications: Hypocalcemia (4) 02/2011

----------INDICATIONS AND USAGE----------
Sensipar is a calcium-sensing receptor agonist indicated for:
- Secondary Hyperparathyroidism (HPT) in patients with chronic kidney disease (CKD) on dialysis. (1.1)
- Hypercalcemia in patients with Parathyroid Carcinoma (PC). (1.2)
- Severe hypercalcemia in patients with primary HPT who are unable to undergo parathyroidectomy. (1.3)

----------DOSAGE AND ADMINISTRATION----------
For all indications, Sensipar should be taken with food or shortly after a meal and should always be taken whole and not divided.
- Secondary HPT in patients with CKD on dialysis (2.1):
  - Starting dose is 30 mg once daily.
  - Titrate dose no more frequently than every 2 to 4 weeks through sequential doses of 30, 60, 90, 120, and 180 mg once daily as necessary to achieve targeted intact parathyroid hormone (iPTH) levels.
  - iPTH levels should be measured no earlier than 12 hours after most recent dose
- Hypercalcemia in patients with PC or severe hypercalcemia in patients with primary HPT (2.2):
  - Starting dose is 30 mg twice daily
  - Titrate dose every 2 to 4 weeks through sequential doses of 30 mg twice daily, 60 mg twice daily, 90 mg twice daily, and 90 mg three or four times daily as necessary to normalize serum calcium levels

----------DOSAGE FORMS AND STRENGTHS----------
Tablets: 30, 60, and 90 mg tablets (3)

----------CONTRAINDICATIONS ----------
Hypocalcemia: Sensipar treatment should not be initiated if serum calcium is less than the lower limit of the normal range. (4, 5.1)

----------WARNINGS AND PRECAUTIONS----------
- Hypocalcemia and/or seizures: May occur due to significant reductions in serum calcium. (5.1, 5.2)
- Isolated, idiosyncratic occurrences of hypotension, worsening heart failure, and/or arrhythmia: Have been reported in patients with impaired cardiac function during Sensipar treatment, which may be mediated by reductions in serum calcium. (5.3)
- Adynamic bone disease: May develop if iPTH levels are suppressed below 100 pg/mL. (5.4)
- Laboratory tests: Serum calcium, serum phosphorus, and iPTH levels should be monitored during the dose initiation, dose titration, and maintenance therapy. (5.6)
- Hepatic Impairment: Cinacalcet exposure is increased in patients with moderate and severe hepatic impairment. Patients should be closely monitored throughout treatment. (5.5, 8.7)

----------ADVERSE REACTIONS----------
The most frequently reported adverse reactions (incidence in patients ≥ 5% in the Sensipar group) were nausea, vomiting, and diarrhea. (6.1, 6.2)

To report SUSPECTED ADVERSE REACTIONS, contact Amgen Medical Information at 1-800-77-AMGEN (1-800-772-6436) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
- Co-administration with a strong CYP3A4 inhibitor may increase serum levels of cinacalcet. Dose adjustment and monitoring of iPTH serum phosphorous and serum calcium may be required. (7.1)
- Cinacalcet is a strong inhibitor of CYP2D6. Dose adjustments may be required for concomitant medications that are predominantly metabolized by CYP2D6 (7.2)

----------USE IN SPECIFIC POPULATIONS----------
- Pregnancy: Sensipar should only be used if the potential benefit justifies the potential risk to the fetus. Pregnancy registry available. (8.1)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 02/2011

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Secondary Hyperparathyroidism

Sensipar is indicated for the treatment of secondary hyperparathyroidism (HPT) in patients with chronic kidney disease (CKD) on dialysis *[see Clinical Studies (14.1)]*.

1.2 Parathyroid Carcinoma

Sensipar is indicated for the treatment of hypercalcemia in patients with parathyroid carcinoma *[see Clinical Studies (14.2)]*.

1.3 Primary Hyperparathyroidism

Sensipar is indicated for the treatment of severe hypercalcemia in patients with primary HPT who are unable to undergo parathyroidectomy *[see Clinical Studies (14.3)]*.

2 DOSAGE AND ADMINISTRATION

Sensipar tablets should be taken whole and should not be divided. Sensipar should be taken with food or shortly after a meal.

Dosage must be individualized.

2.1 Secondary Hyperparathyroidism in Patients with Chronic Kidney Disease on Dialysis

The recommended starting oral dose of Sensipar is 30 mg once daily. Serum calcium and serum phosphorus should be measured within 1 week and intact parathyroid hormone (iPTH) should be measured 1 to 4 weeks after initiation or dose adjustment of Sensipar. Sensipar should be titrated no more frequently than every 2 to 4 weeks through sequential doses of 30, 60, 90, 120, and 180 mg once daily to target iPTH levels of 150 to 300 pg/mL. Serum iPTH levels should be assessed no earlier than 12 hours after dosing with Sensipar.

Sensipar can be used alone or in combination with vitamin D sterols and/or phosphate binders.

During dose titration, serum calcium levels should be monitored frequently and if levels decrease below the normal range, appropriate steps should be taken to increase serum calcium levels, such as by providing supplemental calcium, initiating or increasing the dose of calcium-based phosphate binder, initiating or increasing the dose of vitamin D sterols, or temporarily withholding treatment with Sensipar *[see Warnings and Precautions (5.1, 5.6)]*.

2.2 Parathyroid Carcinoma and Primary Hyperparathyroidism

The recommended starting oral dose of Sensipar is 30 mg twice daily.

The dose of Sensipar should be titrated every 2 to 4 weeks through sequential doses of 30 mg twice daily, 60 mg twice daily, and 90 mg twice daily, and 90 mg 3 or 4 times daily as necessary to normalize serum calcium levels *[see Warnings and Precautions (5.6)]*.

3 DOSAGE FORMS AND STRENGTHS

Sensipar tablets are formulated as light-green, film-coated, oval-shaped tablets marked with “AMG” on one side and “30” or “60” or “90” on the opposite side of the 30 mg, 60 mg, or 90 mg strengths, respectively.

4 CONTRAINDICATIONS

Hypocalcemia: Sensipar treatment should not be initiated if serum calcium is less than the lower limit of the normal range *[see Warnings and Precautions (5.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Hypocalcemia

Sensipar lowers serum calcium and, therefore, patients should be carefully monitored for the occurrence of hypocalcemia. Potential manifestations of hypocalcemia include paresthesias, myalgias, muscle cramping, tetany, and convulsions.

Serum calcium should be measured within 1 week after initiation or dose adjustment of Sensipar. Once the maintenance dose has been established, serum calcium should be measured approximately monthly *[see Dosage and Administration (2.1)]*.

If serum calcium falls below 8.4 mg/dL but remains above 7.5 mg/dL, or if symptoms of hypocalcemia occur, calcium-containing phosphate binders and/or vitamin D sterols can be used to raise serum calcium. If serum calcium falls below 7.5 mg/dL, or if symptoms of hypocalcemia persist and the dose of vitamin D cannot be increased, withhold administration of Sensipar until serum calcium levels reach 8.0 mg/dL and/or symptoms of hypocalcemia have resolved. Treatment should be reinitiated using the next lowest dose of Sensipar *[see Dosage and Administration (2.1)]*.

In 26-week studies of patients with CKD on dialysis, 66% of patients receiving Sensipar compared with 25% of patients receiving placebo developed at least one serum calcium value < 8.4 mg/dL. Less than 1% of patients in each group permanently discontinued study drug due to hypocalcemia.

Sensipar is not indicated for patients with CKD not on dialysis. In patients with secondary HPT and CKD not on dialysis, the long-term safety and efficacy of Sensipar have not been established. Clinical studies indicate that Sensipar-treated patients with CKD not on dialysis have an increased risk for hypocalcemia compared with Sensipar-treated patients with CKD on dialysis, which may be due to lower baseline calcium levels. In a phase 3 study of 32 weeks duration and including 404 patients with CKD not on dialysis (302 cinacalcet, 102 placebo), in which the median dose for cinacalcet was 60 mg per day at the completion of the study, 80% of Sensipar treated patients experienced at least one serum calcium value < 8.4 mg/dL compared with 5% of patients receiving placebo.

5.2 Seizures

In three clinical studies of patients with CKD on dialysis, 5% of the patients in both the Sensipar and placebo groups reported a history of seizure disorder at baseline. During the studies, seizures (primarily generalized or tonic-clonic) were observed in 1.4% (9/656) of Sensipar treated patients and 0.4% (2/470) of placebo-treated patients. Five of the nine Sensipar-treated patients had a history of a seizure disorder and two were receiving anti-seizure medication at the time of their seizure. Both placebo-treated patients had a history of seizure disorder and were receiving antiseizure medication at the time of their seizure. While the basis for the reported difference in seizure rate is not clear, the threshold for seizures is lowered by significant reductions in serum calcium levels. Therefore, serum calcium levels should be closely monitored in patients receiving Sensipar, particularly in patients with a history of a seizure disorder *[see Warnings and Precautions (5.1)]*.

5.3 Hypotension and/or Worsening Heart Failure

In postmarketing safety surveillance, isolated, idiosyncratic cases of hypotension, worsening heart failure, and/or arrhythmia have been reported in patients with impaired cardiac function, in which a causal relationship to Sensipar could not be completely excluded and which may be mediated by reductions in serum calcium levels *[see Adverse Reactions(6.2)]*.

5.4 Adynamic Bone Disease

Adynamic bone disease may develop if iPTH levels are suppressed below 100 pg/mL. One clinical study evaluated bone histomorphometry in patients treated with Sensipar for 1 year. Three patients with mild hyperparathyroid bone disease at the beginning of the study developed adynamic bone disease during treatment with Sensipar. Two of these patients had iPTH levels below 100 pg/mL at multiple time points during the study. In three 6-month, phase 3 studies conducted in patients with CKD on dialysis, 11% of patients treated with Sensipar had mean iPTH values below 100 pg/mL during the efficacy-assessment phase. If iPTH levels decrease below 150 pg/mL in patients treated with Sensipar, the dose of Sensipar and/or vitamin D sterols should be reduced or therapy discontinued.

5.5 Hepatic Impairment

Cinacalcet exposure, as defined by the Area Under the Curve ($AUC_{0\text{-}inf}$), is increased by 2.4 and 4.2 fold in patients with moderate and severe hepatic impairment, respectively. These patients should be monitored throughout treatment with Sensipar *[see Use in Specific Populations (8.7) and Clinical Pharmacology (12.3)]*.

5.6 Laboratory Tests

Secondary Hyperparathyroidism in Patients with Chronic Kidney Disease on Dialysis
Serum calcium and serum phosphorus should be measured within 1 week and iPTH should be measured 1 to 4 weeks after initiation or dose adjustment of Sensipar. Once the maintenance dose has been established, serum calcium and serum phosphorus should be measured approximately monthly, and iPTH every 1 to 3 months *[see Dosage and Administration (2.1)]*. Measurements of PTH during the Sensipar studies were obtained using the Nichols iPTH immunoradiometric assay (IRMA).

In patients with end-stage renal disease, testosterone levels are often below the normal range. In a placebo-controlled study in patients with CKD on dialysis, there were reductions in total and free testosterone in male patients following 6 months of treatment with Sensipar. Levels of total testosterone decreased by a median of 15.8% in the Sensipar-treated patients and by 0.6% in the placebo-treated patients. Levels of free testosterone decreased by a median of 31.3% in the Sensipar-treated patients and by 16.3% in the placebo-treated patients. The clinical significance of these reductions in serum testosterone is unknown.

Patients with Parathyroid Carcinoma or Primary Hyperparathyroidism
Serum calcium should be measured within 1 week after initiation or dose adjustment of Sensipar. Once maintenance dose levels have been established, serum calcium should be measured every 2 months *[see Dosage and Administration (2.2)]*.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Secondary Hyperparathyroidism in Patients with Chronic Kidney Disease on Dialysis
In three double-blind, placebo-controlled clinical trials, 1126 patients with CKD on dialysis received study drug (656 Sensipar, 470 placebo) for up to 6 months. The most frequently reported adverse reactions (incidence of at least 5% in the Sensipar group and greater than placebo) are provided in Table 1. The most frequently reported adverse reactions in the Sensipar group were nausea, vomiting, and diarrhea.

Table 1. Adverse Reaction Incidence (≥ 5%) in Patients on Dialysis

Event*:	Placebo (n = 470) (%)	Sensipar (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
Pain Chest, Non-Cardiac	4	6
Access Infection	4	5

*Included are events that were reported at a greater incidence in the Sensipar group than in the placebo group.

The incidence of serious adverse reactions was similar in the Sensipar and placebo groups (29% vs. 31%, respectively).

12-Month Experience with Sensipar in Secondary Hyperparathyroidism
Two hundred sixty-six patients from two of the phase 3 studies in patients with CKD on dialysis continued to receive Sensipar or placebo treatment in a 6-month, double-blind extension study (12-month total treatment duration). The incidence and nature of adverse reactions in this long term extension study were comparable to those observed in the original phase 3 studies.

Parathyroid Carcinoma and Primary Hyperparathyroidism
The safety profile of Sensipar in these patient populations is generally consistent with that seen in patients with CKD on dialysis. Forty six patients were treated with cinacalcet in a single arm study, 29 with Parathyroid Carcinoma and 17 with intractable PHPT. Nine (20%) of the patients withdrew from the study due to adverse events. The most frequent adverse reactions and the most frequent cause of withdrawal in these patient populations were nausea and vomiting. Severe or prolonged cases of nausea and vomiting can lead to dehydration and worsening hypercalcemia so careful monitoring of electrolytes is recommended in patients with these symptoms.

Eight patients died while on study, 7 with parathyroid carcinoma (24%) and 1 (6%) with intractable PHPT. Causes of death were cardiovascular (5 patients), multi-organ failure (1 patient), gastrointestinal hemorrhage (1 patient) and metastatic carcinoma (1 patient). Adverse events of hypocalcemia were reported in three patients (7%).

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