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, for oral use
Initial US Approval: 2004

----------RECENT MAJOR CHANGES----------

Warnings and Precautions, Hypocalcemia (5.1)	5/2017
Warnings and Precautions, Upper Gastrointestinal Bleeding (5.2)	3/2017
Warnings and Precautions, Hypotension, Worsening Heart Failure and/or Arrhythmias (5.3)	5/2017

----------INDICATIONS AND USAGE----------

Sensipar is a calcium-sensing receptor agonist indicated for:

- Secondary Hyperparathyroidism (HPT) in adult patients with chronic kidney disease (CKD) on dialysis. (1.1)
  Limitations of Use: Sensipar is not indicated for use in patients with CKD who are not on dialysis
- Hypercalcemia in adult patients with Parathyroid Carcinoma (PC). (1.2)
- Hypercalcemia in adult patients with primary HPT for whom parathyroidectomy would be indicated on the basis of serum calcium levels, but who are unable to undergo parathyroidectomy. (1.3)

----------DOSAGE AND ADMINISTRATION----------

- Sensipar tablets should be taken with food or shortly after a meal (2.1).
- Tablets should always be taken whole and not divided (2.1)
- Secondary HPT in patients with CKD on dialysis (2.2):
  - 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 hypercalcemia in patients with primary HPT (2.3):
  - 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.
- Once the maintenance dose has been established, monitor serum calcium approximately monthly for patients with secondary HPT and every 2 months for patients with PC or primary HPT (2.4)

----------DOSAGE FORMS AND STRENGTHS----------

- Tablets: 30, 60, and 90 mg tablets (3)

----------CONTRAINDICATIONS ----------

Sensipar treatment initiation is contraindicated if serum calcium is less than the lower limit of the normal range. (4, 5.1)

----------WARNINGS AND PRECAUTIONS----------

- *Hypocalcemia:* Life threatening events and fatal outcomes were reported. Hypocalcemia can prolong QT interval, lower the threshold for seizures, and cause hypotension, worsening heart failure, and/or arrhythmia. Monitor serum calcium carefully for the occurrence of hypocalcemia during treatment (2.4, 5.1)
- *Upper Gastrointestinal (GI) Bleeding:* Patients with risk factors for upper GI bleeding may be at increased risk. Monitor patients and promptly evaluate and treat any suspected GI bleeding. (5.2)
- *Hypotension, Worsening Heart Failure and/or Arrhythmias*: In postmarketing safety surveillance, isolated, idiosyncratic cases of hypotension, worsening heart failure, and/or arrhythmia have been reported in patients with impaired cardiac function. (5.3)
- *Adynamic Bone Disease*: May develop if iPTH levels are suppressed below 100 pg/mL. (5.4)

----------ADVERSE REACTIONS----------

The most common adverse reactions (i.e., ≥ 25%) associated with Sensipar were nausea and vomiting. (6)

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 phosphorus 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----------

- Pediatric Use: A fatal outcome was reported in a pediatric clinical trial patient with severe hypocalcemia. Sensipar is not indicated for use in pediatric patients. (8.4)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 5/2017

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 adult patients with chronic kidney disease (CKD) on dialysis *[see Clinical Studies (14.1)]*.

Limitations of Use:

Sensipar is not indicated for use in patients with CKD who are not on dialysis because of an increased risk of hypocalcemia *[see Warnings and Precautions (5.1)]*.

1.2 Parathyroid Carcinoma

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

1.3 Primary Hyperparathyroidism

Sensipar is indicated for the treatment of hypercalcemia in adult patients with primary HPT for whom parathyroidectomy would be indicated on the basis of serum calcium levels, but who are unable to undergo parathyroidectomy *[see Clinical Studies (14.3)]*.

2 DOSAGE AND ADMINISTRATION

2.1 Administration

Sensipar should be taken with food or shortly after a meal.

Sensipar tablets are administered orally and should always be taken whole and not chewed, crushed, or divided.

2.2 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 *[see Dosage and Administration (2.3)]*. 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 Dosage and Administration (2.4) and Warnings and Precautions (5.1)]*.

2.3 Patients with 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. Serum calcium should be measured within 1 week after initiation or dose adjustment of Sensipar *[see Dosage and Administration (2.4) and Warnings and Precautions (5.1)]*.

2.4 Monitoring for Hypocalcemia

Once the maintenance dose has been established, serum calcium should be measured approximately monthly for patients with secondary hyperparathyroidism with CKD on dialysis, and every 2 months for patients with parathyroid carcinoma or primary hyperparathyroidism *[see Dosage and Administration (2.2, 2.3)]*.

For secondary hyperparathyroidism patients with CKD on dialysis, 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 (2.2)]*.

3 DOSAGE FORMS AND STRENGTHS

Sensipar is available as film-coated tablets.

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

Sensipar treatment initiation is contraindicated 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 can lead to hypocalcemia *[see Adverse Reactions (6.1)]*. Significant lowering of serum calcium can cause paresthesias, myalgias, muscle spasms, tetany, seizures, QT interval prolongation and ventricular arrhythmia. Life threatening events and fatal outcomes associated with hypocalcemia have been reported in patients treated with Sensipar, including in pediatric patients. The safety and effectiveness of Sensipar have not been established in pediatric patients *[see Pediatric Use (8.4)]*.

Sensipar is not indicated for patients with CKD not on dialysis *[see Indications and Usage (1)]*. 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.

QT Interval Prolongation and Ventricular Arrhythmia

Decreases in serum calcium can also prolong the QT interval, potentially resulting in ventricular arrhythmia. Cases of QT prolongation and ventricular arrhythmia have been reported in patients treated with Sensipar. Patients with congenital long QT syndrome, history of QT interval prolongation, family history of long QT syndrome or sudden cardiac death, and other conditions that predispose to QT interval prolongation and ventricular arrhythmia may be at increased risk for QT interval prolongation and ventricular arrhythmias if they develop hypocalcemia due to Sensipar. Closely monitor corrected serum calcium and QT interval in patients at risk receiving Sensipar.

Seizures

In clinical studies, seizures (primarily generalized or tonic-clonic) were observed in 1.4% (43/3049) of Sensipar-treated patients and 0.7% (5/687) of placebo-treated patients. 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. Monitor serum calcium levels in patients with seizure disorders receiving Sensipar.

Concurrent administration of Sensipar with calcium-lowering drugs including other calcium-sensing receptor agonists could result in severe hypocalcemia. Closely monitor serum calcium in patients receiving Sensipar and concomitant therapies known to lower serum calcium levels.

Educate patients on the symptoms of hypocalcemia and advise them to contact a healthcare provider if they occur.

If corrected serum calcium falls below the lower limit of normal or symptoms of hypocalcemia develop, start or increase calcium supplementation (including calcium, calcium-containing phosphate binders, and/or vitamin D sterols or increases in dialysate calcium concentration). Sensipar dose reduction or discontinuation of Sensipar may be necessary *[see Dosage and Administration (2.2)]*.

5.2 Upper Gastrointestinal Bleeding

Cases of gastrointestinal bleeding, mostly upper gastrointestinal bleeding, have occurred in patients using calcimimetics, including Sensipar, from postmarketing and clinical trial sources. The exact cause of GI bleeding in these patients is unknown.

Patients with risk factors for upper GI bleeding (such as known gastritis, esophagitis, ulcers or severe vomiting) may be at increased risk for GI bleeding when receiving Sensipar treatment. Monitor patients for worsening of common GI adverse reactions of nausea and vomiting associated with Sensipar *[see Adverse Reactions (6.1)]* and for signs and symptoms of GI bleeding and ulcerations during Sensipar therapy. Promptly evaluate and treat any suspected GI bleeding.

5.3 Hypotension, Worsening Heart Failure and/or Arrhythmias

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.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of labeling:

- Hypocalcemia *[see Warnings and Precautions (5.1)]*
- Upper Gastrointestinal Bleeding *[see Warnings and Precautions (5.2)]*
- Hypotension, Worsening Heart Failure and/or Arrhythmias [*see Warnings and Precautions (5.3)]*

- Adynamic Bone Disease *[see Warnings and Precautions (5.4)]*

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 are listed in Table 1.

Seizures were observed in 1.4% (13/910) of Sensipar-treated patients and 0.7% (5/641) of placebo-treated patients across all completed placebo controlled trials.

Table 1. Adverse Reactions with Frequency ≥ 5% in Patients on Dialysis in Short-Term Studies for up to 6 Months

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
Dialysis Access Site Infection	4	5

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

In a randomized, double-blind placebo controlled study of 3883 patients with secondary HPT and CKD receiving dialysis in which patients were treated for up to 64 months (mean duration of treatment was 21 months in the Sensipar group), the most frequently reported adverse reactions (incidence of ≥ 5% in the Sensipar group and a difference ≥ 1% compared to placebo) are listed in Table 2.

Table 2. Frequency of Adverse Reactions in Dialysis Patients Treated for up to 64 Months in a Long-Term Study[1]

	Placebo (n = 1923)	Sensipar (n = 1938)
	3699 subject-years	4044 subject-years
Percent of subjects reporting Adverse Reactions (%)	90.9	93.2
Nausea	15.5	29.1
Vomiting	13.7	25.6
Diarrhea	18.7	20.5
Dyspnea	11.5	13.4
Cough	9.8	11.7

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.