LOUISIANA BLUE

Sensipar®, generics (cinacalcet)

Policy # 00631
Original Effective Date: 01/01/2019
Current Effective Date: 04/01/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider brand or generic Sensipar®‡ (cinacalcet) for the treatment of hypercalcemia to be **eligible for coverage**** when the patient selection criteria are met.

Patient Selection Criteria

Coverage eligibility for brand or generic Sensipar (cinacalcet) will be considered when the following criteria are met:

1. Patient has a serum calcium above or within the normal range as defined by the laboratory reference value AND meets one of the following (a, b, c, or d):
    a. Has a diagnosis of secondary hyperparathyroidism; AND
        i. Has an intact parathyroid hormone (iPTH) level at least two times the upper limit of normal as defined by the laboratory reference value measured on two separate occasions; AND
        *(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
        ii. Has chronic kidney disease (CKD); AND
        iii. Is dependent upon dialysis; OR
    b. Has a diagnosis of parathyroid carcinoma; OR
    c. Has a diagnosis of primary hyperparathyroidism; AND
        i. Has a serum calcium above the normal range; AND
        ii. Is not a candidate for parathyroidectomy; OR
    d. Has a diagnosis of hyperparathyroidism after renal transplant (tertiary hyperparathyroidism); AND
        i. Has received a kidney transplant; AND

ii. Has tried vitamin D analogues to treat secondary hyperparathyroidism and the trial has failed or is limited by hypercalcemia; AND
iii. The patient has an iPTH level above the normal range as defined by the laboratory reference value; AND

2. If the request is for brand Sensipar, patient has tried and failed (e.g. intolerance or inadequate response), GENERIC cinacalcet unless there is clinical evidence or patient history that suggests the use of GENERIC cinacalcet will be ineffective or cause an adverse reaction to the patient.
*(Note: this specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Sensipar (cinacalcet) for the treatment of secondary hyperparathyroidism when the patient does NOT have an iPTH level at least two times the upper limit of normal measured on two separate occasions to be **not medically necessary.****

Based on review of available data, the Company considers the use of brand Sensipar when the patient has not tried and failed GENERIC cinacalcet to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers Sensipar (cinacalcet) when patient selection criteria are not met (except for the criteria considered to be **not medically necessary**) to be **investigational.***

Background/Overview

Sensipar is a calcium-sensing receptor agonist (calcimimetic) indicated for the treatment of secondary hyperparathyroidism in adult patients with CKD on dialysis. It is also indicated for the treatment of hypercalcemia in adult patients with parathyroid carcinoma and for the treatment of hypercalcemia in adult patients with primary hyperparathyroidism for whom parathyroidectomy would be indicated on the basis of serum calcium levels, but who are unable to undergo parathyroidectomy. In addition to the Food and Drug Administration (FDA)-labeled indications, Sensipar is commonly used for the treatment of tertiary hyperparathyroidism in patients who have received a kidney transplant. It is dosed differently for each indication, but each dose should be titrated to response. Sensipar tablets should be administered with food or shortly after a meal and should not be chewed, crushed, or divided.

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The Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guidelines (2017) for the treatment of CKD-mineral bone disorder (MBD) recommends the use of Sensipar, calcitriol, vitamin D analogues, or a combination of these agents in CKD stage 5D (dialysis) patients with elevated or rising parathyroid hormone (PTH). The guidelines recognize that there are no randomized controlled trials showing that treatment to achieve a specific PTH level results in improved outcomes. There is no established "cause and effect" relationship between the measured biochemical variables and observed outcomes. Therefore, the guidelines recommend interpreting changes in PTH in conjunction with calcium and phosphorous levels to guide therapeutic decisions. Overall, in patients with CKD stage 5D, the KDIGO guidelines suggest maintaining iPTH levels in the range of approximately two to nine times the upper limit of normal (ULN) for the assay. Any marked changes in PTH levels in either direction within this range should prompt an initiation or change in therapy to avoid progression to iPTH levels outside of this range. These guidelines also note that although Sensipar is not approved for the treatment of hyperparathyroidism in kidney transplant recipients, it is used in these patients, especially those with significant hypercalcemia.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Sensipar is indicated for the treatment of secondary hyperparathyroidism in adult patients with CKD on dialysis. It is not indicated for use in patients with CKD who are not on dialysis because of an increased risk of hypocalcemia. Sensipar is also indicated for the treatment of hypercalcemia in adult patients with parathyroid carcinoma and for the treatment of hypercalcemia in adult patients with primary hyperparathyroidism for whom parathyroidectomy would be indicated on the basis of serum calcium levels, but who are unable to undergo parathyroidectomy.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Secondary Hyperparathyroidism in Patients with CKD on Dialysis

Three 6-month, multicenter, randomized, double-blind, placebo-controlled clinical studies of similar design were conducted in patients with CKD on dialysis. A total of 665 patients were randomized to Sensipar and 471 patients to placebo. At study entry, 66% of the patients were receiving vitamin D sterols and 93% were receiving phosphate binders. Sensipar was initiated at a dose of 30 mg once daily and titrated every 3 or 4 weeks to a maximum dose of 180 mg once daily to achieve an iPTH of $\leq$250 pg/mL. If a patient experienced symptoms of hypocalcemia or had a serum calcium <8.4 mg/dL, calcium supplements and/or calcium-based phosphate binders could be increased. Approximately 70% of patients in the Sensipar arm and 80% of the patients in the placebo arm

completed the 6-month studies. In the primary efficacy analysis of patients who completed the studies, 40% of the patients on Sensipar and 5% of placebo-treated patients achieved an iPTH ≤250 pg/mL ($p<0.001$). These studies showed that Sensipar reduced iPTH while lowering Ca x P, calcium, and phosphorus levels. The median dose of Sensipar at the completion of the studies was 90 mg. Patients with milder disease typically required lower doses.

Parathyroid Carcinoma
29 patients with parathyroid carcinoma were enrolled in a single-arm, open-label study. The study consisted of two phases, a dose-titration phase and a maintenance phase. Patients initially received 30 mg of Sensipar twice daily and then were titrated every 2 weeks to a maximum dose of 90 mg four times daily. Dosage escalation during the variable-length titration phase continued until the serum calcium concentration was ≤10 mg/dL, the patient reached the highest possible dosage, or adverse events precluded further dosage increases. The baseline mean serum calcium was 14.1 mg/dL. At the end of the titration phase, the mean serum calcium was 12.4 mg/dL, which represents a mean reduction of 1.7 mg/dL from baseline.

Hypercalcemia due to Primary Hyperparathyroidism
17 patients with severe hypercalcemia due to primary hyperparathyroidism, who had failed or had contraindications to parathyroidectomy, participated in an open-label, single-arm study. The study consisted of two phases, a dose-titration phase and a maintenance phase. In this trial, severe hypercalcemia was defined as a screening serum calcium level of >12.5 mg/dL. Patients initially received 30 mg Sensipar twice daily and then were titrated every 2 weeks to a maximum dose of 90 mg 4 times daily. Dosage escalation during the variable-length titration phase continued until the serum calcium concentration was ≤10 mg/mL, the patient reached the highest possible dosage, or adverse events precluded further dosage increases. At baseline, the mean serum calcium was 12.7 mg/dL. At the end of the titration phase, the mean serum calcium was 10.4 mg/dL which represents a mean reduction of 2.3 mg/dL from baseline. The median dose of Sensipar at the completion of the study was 60 mg/day.

Tertiary Hyperparathyroidism Post-Renal Transplant
A 2012 meta-analysis reviewed 21 studies with 411 kidney transplant patients treated with Sensipar for hyperparathyroidism (HPT). The treatment duration varied from 3 to 24 months, with a wide range of doses. None of the trials included in the analysis were randomized controlled trials. The meta-analysis concluded that Sensipar was an effective treatment option for post-renal transplant patients with HPT; Sensipar decreased calcium levels by 1.14 mg/dL, increased phosphorous levels by 0.46 mg/dL and decreased iPTH levels by 102 pg/mL. All of these results were statistically significant. Another retrospective observational study reported on Sensipar use for persistent HPT in 23 kidney transplant patients after long-term follow-up (median 53 months). Patients had been persistently hypercalcemic for > 12 months after transplant and before starting Sensipar treatment. Three months after Sensipar initiation, there was a significant reduction in calcium and an increase in phosphorus levels toward normal levels that were maintained throughout the follow-up period.

There were no changes in renal function. A review article also outlined a treatment algorithm for the management of hypercalcemia with Sensipar in post-renal transplant patients based on the available published data and clinical experience.

A 2014 randomized, double-blind, placebo-controlled, multicenter, Phase III study (n = 114) compared Sensipar with placebo for the treatment of hypercalcemia in patients with persistent HPT following renal transplant. Eligible patients were between 9 weeks and 24 months post-transplant, had stable renal function, a corrected serum Ca > 10.5 mg/dL and an iPTH > 100 pg/mL. Between 22 and 26 weeks of Sensipar therapy (dosing within current labeling guidelines), 78.9% of patients in the Sensipar group achieved the primary endpoint, a mean corrected total serum Ca level of < 10.2 mg/dL, compared with only 3.5% of patients receiving placebo ($P < 0.001$). Therapy with Sensipar did not significantly improve bone mineral density at the femoral neck when measured at Week 52 (Sensipar vs. placebo, $P = 0.266$). However, Sensipar significantly increased phosphorous levels and decreased iPTH levels at Week 26.

References

1. Sensipar [package insert]. Amgen Inc. Thousand Oaks, CA. May 2017
2. Sensipar PA policy. Express Scripts. February 2018.

Policy History

Original Effective Date: 01/01/2019
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08/09/2018	Medical Policy Committee review
08/15/2018	Medical Policy Implementation Committee approval. New policy.
06/06/2019	Medical Policy Committee review
06/19/2019	Medical Policy Implementation Committee approval. Criteria updated to allow coverage with normocalcemia under certain conditions and to clarify the term tertiary hyperparathyroidism.
03/05/2020	Medical Policy Committee review
03/11/2020	Medical Policy Implementation Committee approval. Title changed from "Sensipar (cinacalcet)" to "Sensipar, generics (cinacalcet)". Generic added to policy with new criterion requiring trial of generic prior to brand.
03/04/2021	Medical Policy Committee review
03/10/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/04/2021	Medical Policy Committee review
03/10/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

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03/03/2022	Medical Policy Committee review
03/09/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/02/2023	Medical Policy Committee review
03/08/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/07/2024	Medical Policy Committee review
03/13/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/06/2025	Medical Policy Committee review
03/12/2025	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 03/2026

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and

C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.