

# TARGET

## The TARGET study:

# Combined Therapy with Cinacalcet and Low Doses of Vitamin D Sterols in Patients with Moderate to Severe Secondary Hyperparathyroidism

*"...cinacalcet was shown to lower serum calcium and phosphorus concentrations while maintaining control of plasma PTH levels when used together with low doses of vitamin D sterols."*

—Chertow et al<sup>1</sup>

**Sensipar<sup>®</sup> is indicated for the treatment of secondary hyperparathyroidism (HPT) in patients with chronic kidney disease (CKD) on dialysis.**

### **Important Safety Information**

- Sensipar<sup>®</sup> treatment should not be initiated if serum calcium is less than the lower limit of the normal range (8.4 mg/dL).
- Sensipar<sup>®</sup> lowers serum calcium; therefore, it is important that patients are carefully monitored for the occurrence of hypocalcemia.
- Significant reductions in calcium may lower the threshold for seizures. Secondary hyperparathyroidism (HPT) patients, particularly those with a history of seizure disorder, should be carefully monitored for the occurrence of low serum calcium or symptoms of hypocalcemia.
- In Sensipar<sup>®</sup> postmarketing use, isolated, idiosyncratic cases of hypotension, worsening heart failure, and/or arrhythmia were reported in patients with impaired cardiac function. The causal relationship to Sensipar<sup>®</sup> therapy could not be completely excluded and may be mediated by reductions in serum calcium levels.
- Adynamic bone disease may develop if intact parathyroid hormone (iPTH) levels are suppressed below 100 pg/mL.
- Patients with moderate to severe hepatic impairment should be monitored throughout treatment with Sensipar<sup>®</sup>, as cinacalcet exposure assessed by area under the curve (AUC) was higher than in patients with normal hepatic function.
- Serum calcium and serum phosphorus should be measured within 1 week and PTH should be measured 1 to 4 weeks after initiation or dose adjustment of Sensipar<sup>®</sup>. Once the maintenance dose has been established, serum calcium and serum phosphorus should be measured approximately monthly, and PTH every 1 to 3 months.
- The most commonly reported side effects were nausea, vomiting, and diarrhea.

*Please refer to the accompanying Sensipar<sup>®</sup> Package Insert for full prescribing information.*

**TARGET** = Treatment Strategies to **Achieve Recommended KDOQI™ Goals in ESRD Patients on Cinacalcet**.

KDOQI™ is a trademark of the National Kidney Foundation, Inc.

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**Sensipar<sup>®</sup>**  
(cinacalcet) Tablets  
30mg·60mg·90mg

## Study objective<sup>1</sup>

- To determine whether treatment with Sensipar® combined with low doses of vitamin D sterols improves control of secondary HPT laboratory parameters\*

## Study design<sup>1</sup>

- TARGET was a multicenter, single-arm, open-label study

The TARGET study enrolled 444 patients ≥ 18 years and receiving dialysis for ≥ 3 months

- Patients had iPTH 300–800 pg/mL<sup>†</sup> and Ca ≥ 8.4 mg/dL
- Patients with ongoing use of oral vitamin D sterols were excluded

After a 30-day screening period, Sensipar® was initiated at 30 mg once daily and titrated sequentially every 2 weeks<sup>‡</sup> during an 8-week dose-titration phase to achieve iPTH ≤ 300 pg/mL

Vitamin D dose was reduced to 2 µg<sup>§</sup>/treatment at week 2 (day 15) per the protocol-specified TARGET treatment algorithm

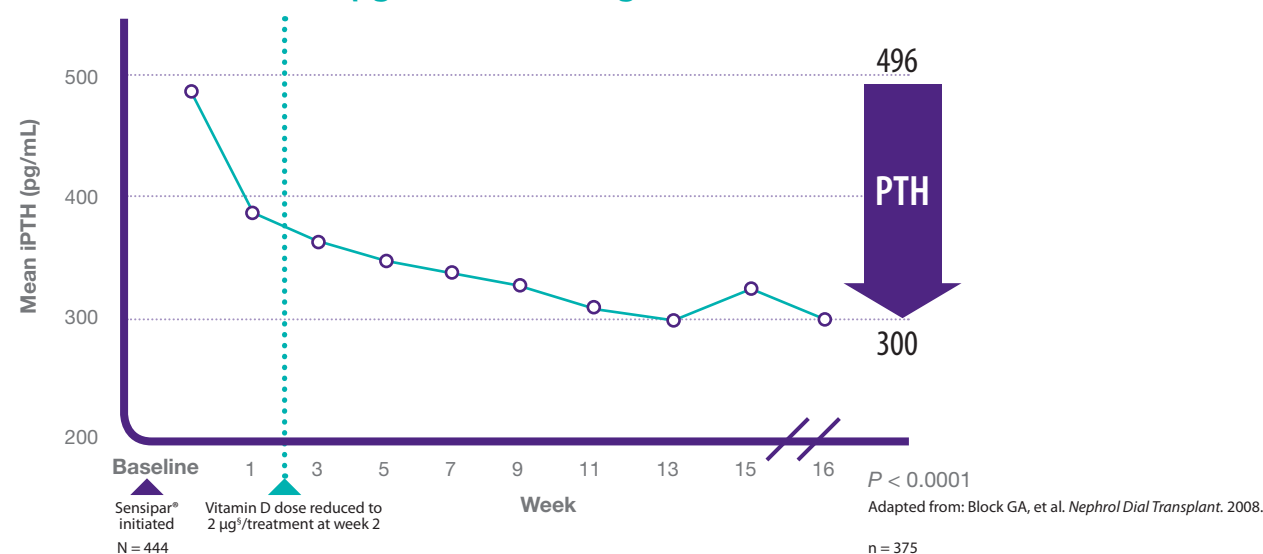
The 2 µg<sup>§</sup>/treatment dose at week 2 was a 71% reduction from the mean baseline vitamin D dose of 6.9 µg/treatment.

See insert in pocket for description of treatment algorithm.

- "...doses were reduced during the second week of the dose-titration phase to an amount considered to be approximately equivalent to the endogenous production rate for calcitriol among persons with normal renal function." —Block et al<sup>1</sup>

## Results<sup>1</sup>

Initiating Sensipar® at iPTH > 300 pg/mL and reducing vitamin D to 2 µg<sup>§</sup> resulted in significant PTH reductions



Please see Important Safety Information on front cover.

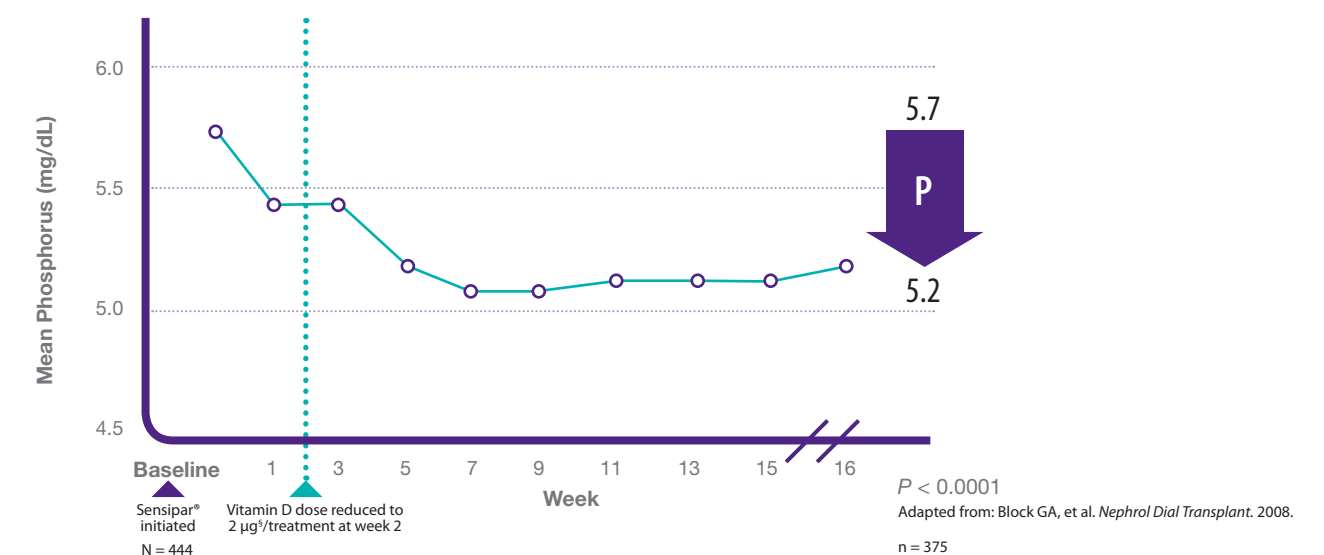
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\*Treatment goals defined as iPTH ≤ 300 pg/mL and Ca x P < 55 mg<sup>2</sup>/dL<sup>2</sup>.

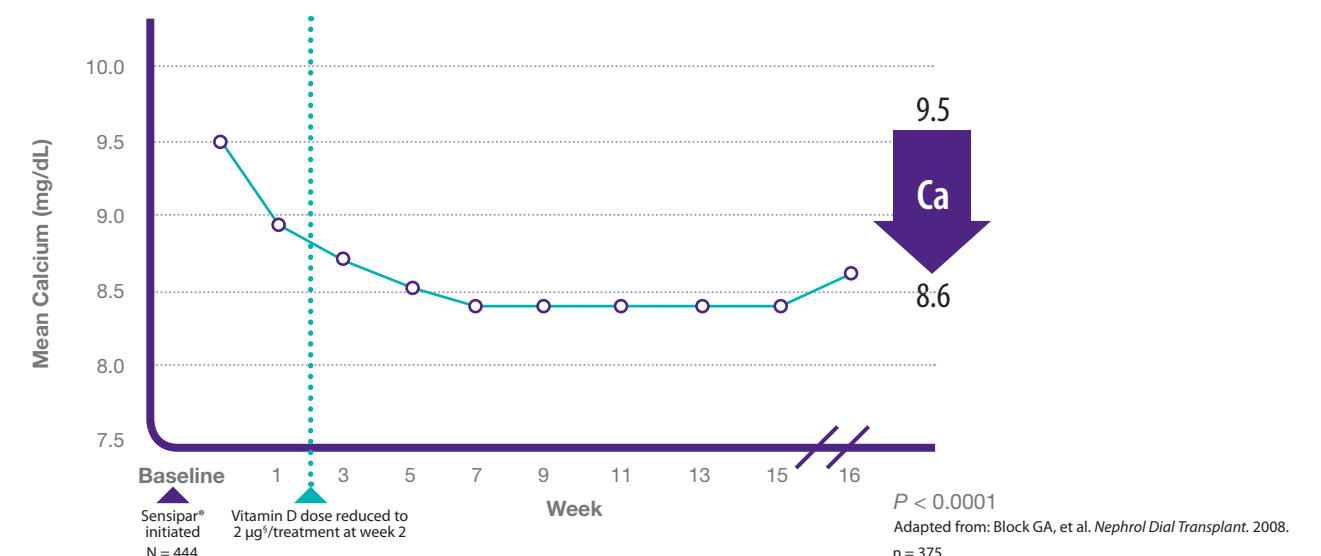
<sup>†</sup>When the TARGET trial was designed and implemented, the Nichols bioactive PTH (biPTH) assay was used to determine PTH levels. Since the biPTH assay is no longer available, biPTH values are reported as iPTH, using the conversion factor of approximately 0.54. Based on this conversion, biPTH 160–430 pg/mL ≈ iPTH 300–800 pg/mL.<sup>2</sup>

## Results<sup>1</sup> (cont'd)

Initiating Sensipar® at iPTH > 300 pg/mL and reducing vitamin D to 2 µg<sup>§</sup> resulted in significant phosphorus reductions



Initiating Sensipar® at iPTH > 300 pg/mL and reducing vitamin D to 2 µg<sup>§</sup> resulted in calcium reductions



- Mean Sensipar® dose was 70 mg/day

## Reported adverse events<sup>1</sup>

- The most common adverse events were nausea (28%), vomiting (23%), diarrhea (19%), headache (11%), and dizziness (11%)
- Less than 1% of patients discontinued therapy due to hypocalcemia (Ca < 7.5 mg/dL)

## Additional Safety Information

- Sensipar® lowers serum calcium; therefore, it is important that patients have a serum calcium ≥ 8.4 mg/dL when initiating therapy.
- Sensipar® can be used alone or in combination with vitamin D sterols and/or phosphate binders.

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<sup>‡</sup>Patients were titrated sequentially every 2 weeks to a maximum dose of 180 mg once daily or until an adverse event precluded a dosage increase. Doses of Sensipar® could be decreased if iPTH values on 2 consecutive study visits were < 150 pg/mL and treatment with vitamin D had already been discontinued.

<sup>§</sup>2.0 µg paricalcitol or its equivalents. Paricalcitol equivalents defined as paricalcitol 2.0 µg = doxercalciferol 1.0 µg = calcitriol 0.5 µg.

iPTH = intact parathyroid hormone; Ca = calcium; P = phosphorus.

## Key points<sup>1</sup>

- Despite the use of phosphate binders, vitamin D based therapy of secondary HPT can lead to increases in serum calcium and phosphorus
- Initiating Sensipar<sup>®</sup> at iPTH >300 pg/mL and Ca ≥ 8.4 mg/dL, then reducing vitamin D dose to 2 µg\* per treatment at week 2 resulted in significant reductions in PTH, phosphorus, and calcium in patients on dialysis with secondary HPT
- Reductions in PTH, phosphorus, and calcium were maintained over 16 weeks

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### Important Safety Information

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- Sensipar<sup>®</sup> lowers serum calcium; therefore, it is important that patients are carefully monitored for the occurrence of hypocalcemia.
- Significant reductions in calcium may lower the threshold for seizures. Secondary hyperparathyroidism (HPT) patients, particularly those with a history of seizure disorder, should be carefully monitored for the occurrence of low serum calcium or symptoms of hypocalcemia.
- In Sensipar<sup>®</sup> postmarketing use, isolated, idiosyncratic cases of hypotension, worsening heart failure, and/or arrhythmia were reported in patients with impaired cardiac function. The causal relationship to Sensipar<sup>®</sup> therapy could not be completely excluded and may be mediated by reductions in serum calcium levels.
- Adynamic bone disease may develop if intact parathyroid hormone (iPTH) levels are suppressed below 100 pg/mL.
- Patients with moderate to severe hepatic impairment should be monitored throughout treatment with Sensipar<sup>®</sup>, as cinacalcet exposure assessed by area under the curve (AUC) was higher than in patients with normal hepatic function.
- Serum calcium and serum phosphorus should be measured within 1 week and PTH should be measured 1 to 4 weeks after initiation or dose adjustment of Sensipar<sup>®</sup>. Once the maintenance dose has been established, serum calcium and serum phosphorus should be measured approximately monthly, and PTH every 1 to 3 months.
- The most commonly reported side effects were nausea, vomiting, and diarrhea.

*Please refer to the accompanying Sensipar<sup>®</sup> Package Insert for full prescribing information.*

**References:** **1.** Block GA, Zeig S, Sugihara J, et al; for the TARGET investigators. Combined therapy with cinacalcet and low doses of vitamin D sterols in patients with moderate to severe secondary hyperparathyroidism. *Nephrol Dial Transplant*. 2008;23(7):2311-2318. **2.** Martin KJ, Jüppner H, Sherrard DJ, et al. First- and second-generation immunometric PTH assays during treatment of hyperparathyroidism with cinacalcet HCl. *Kidney Int*. 2005;68(3):1236-1243.

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30mg · 60mg · 90mg

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## The TARGET treatment algorithm<sup>1</sup>

### Identify secondary HPT patient

On dialysis  $\geq$  3 months  
Ca  $\geq$  8.4 mg/dL  
iPTH 300-800 pg/mL

### Initiate and titrate Sensipar®

Maintain phosphate binder dose  
Maintain type of vitamin D  
Initiate Sensipar® at 30 mg/day

### Adjust dosing

At week 2, reduce dose of vitamin D to 2  $\mu$ g\*/treatment (6  $\mu$ g/week)

Titrate Sensipar® sequentially (30–180 mg/day) to achieve iPTH 300 pg/mL<sup>†</sup>

Increase vitamin D if Ca < 8.4 mg/dL or iPTH > 500 pg/mL after max doses of Sensipar® are reached

\*2.0  $\mu$ g paricalcitol or its equivalents. Paricalcitol equivalents defined as paricalcitol 2.0  $\mu$ g = doxercalciferol 1.0  $\mu$ g = calcitriol 0.5  $\mu$ g.

<sup>†</sup>Unless patient experienced an adverse event that precluded a dosage increase. Doses of Sensipar® could be decreased if iPTH values on two consecutive study visits were 150 pg/mL and treatment with vitamin D had already been discontinued.

### Additional Safety Information

- Sensipar® lowers serum calcium; therefore, it is important that patients have a serum calcium  $\geq$  8.4 mg/dL when initiating therapy.
- 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 re-initiated using the next lowest dose of Sensipar®.

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