

Only one calcimimetic lowers and maintains key sHPT lab values with IV administration you control¹



sHPT = secondary hyperparathyroidism;
IV = intravenous; P = phosphate;
PTH = parathyroid hormone; cCa =
corrected calcium.

**Not an actual Parsabiv® vial.
The displayed vial is for
illustrative purposes only.**

Indication

Parsabiv® (etelcalcetide) is indicated for the treatment of secondary hyperparathyroidism (HPT) in adult patients with chronic kidney disease (CKD) on hemodialysis.

Limitations of Use:

Parsabiv® has not been studied in adult patients with parathyroid carcinoma, primary hyperparathyroidism, or with CKD who are not on hemodialysis and is not recommended for use in these populations.

Important Safety Information for Parsabiv®

Parsabiv® is contraindicated in patients with known hypersensitivity to etelcalcetide or any of its excipients. Hypersensitivity reactions, including face edema and anaphylactic reaction, have occurred.

Please see additional Important Safety Information on page 13.

 **Parsabiv**
(etelcalcetide) Injection for intravenous use
2.5mg/0.5mL | 5mg/1mL | 10mg/2mL

Getting to know Parsabiv®

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What are the fundamentals of Parsabiv®?



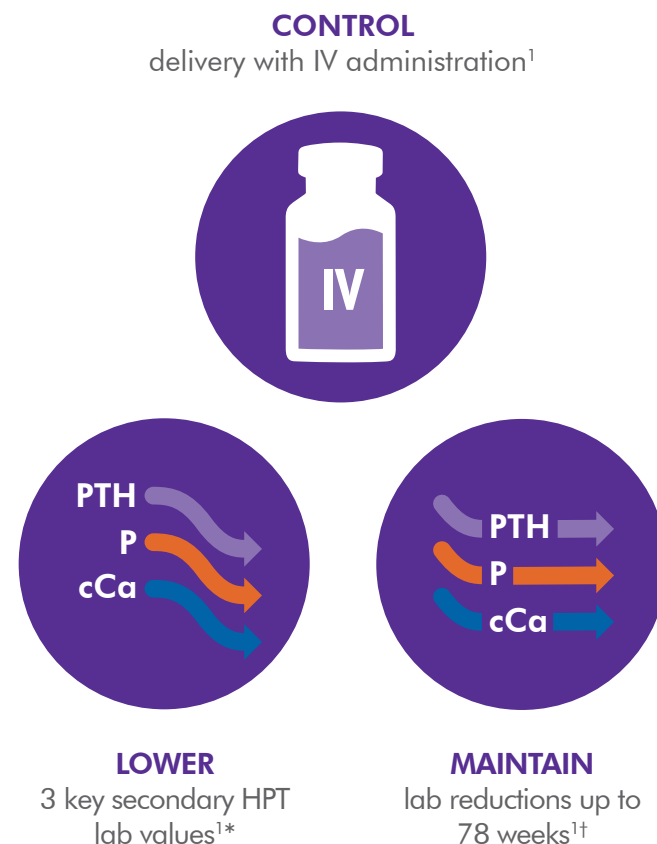
Not an actual Parsabiv® vial. The displayed vial is for illustrative purposes only.

Important Safety Information for Parsabiv®

Parsabiv® lowers serum calcium and can lead to hypocalcemia, sometimes severe.

Please see additional Important Safety Information for Parsabiv® and Sensipar® on page 13.

Parsabiv® gives you control over calcimimetic delivery at the end of hemodialysis¹



^{*}Results are combined from two 26-week, randomized, double-blind, placebo-controlled studies comparing Parsabiv® with placebo in patients with chronic kidney disease (CKD) on hemodialysis.

[†]Open-label extension (OLE): data pooled for patients receiving Parsabiv® across two placebo-controlled parent studies and a subsequent OLE study, starting from the baseline of the parent study until the end or the prespecified cutoff date of the OLE study, whichever was earlier.²

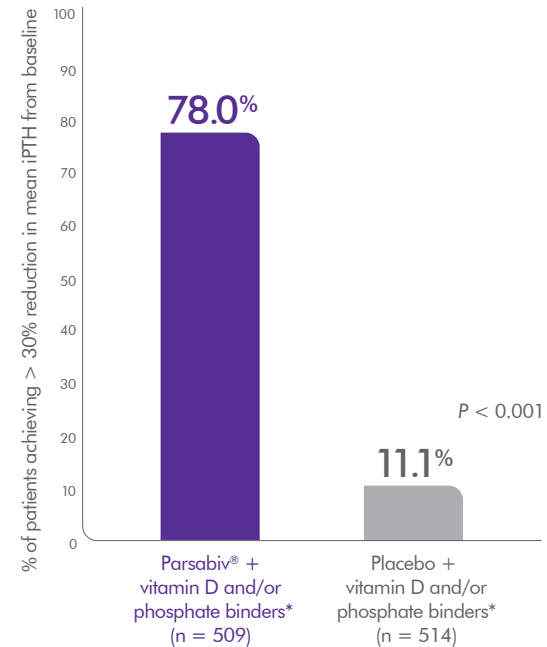
What effect does Parsabiv® have on PTH levels?

Important Safety Information for Parsabiv®

Significant lowering of serum calcium can cause QT interval prolongation and ventricular arrhythmia.

Please see additional Important Safety Information for Parsabiv® and Sensipar® on page 13.

Approximately 7 times more patients given Parsabiv® achieved > 30% reduction in mean PTH vs placebo³



Results are combined from two 26-week, randomized, double-blind, placebo-controlled studies comparing Parsabiv® with placebo in patients with chronic kidney disease (CKD) on hemodialysis with iPTH > 400 pg/mL and corrected calcium $\geq$ 8.3 mg/dL (N = 1023). Patients in both treatment arms could be treated with vitamin D sterols and/or phosphate binders. Mean baseline iPTH in the Parsabiv® group and placebo group were 847 pg/mL and 836 pg/mL, respectively. The primary endpoint of each study was the proportion of patients who achieved a > 30% reduction from baseline in mean iPTH during the efficacy assessment period (defined as weeks 20 through 27, inclusive).^{1,2,4}

*Vitamin D and/or phosphate binders, if prescribed.⁴

When could I expect to see changes in PTH levels after initiating Parsabiv®?

Important Safety Information for Parsabiv®

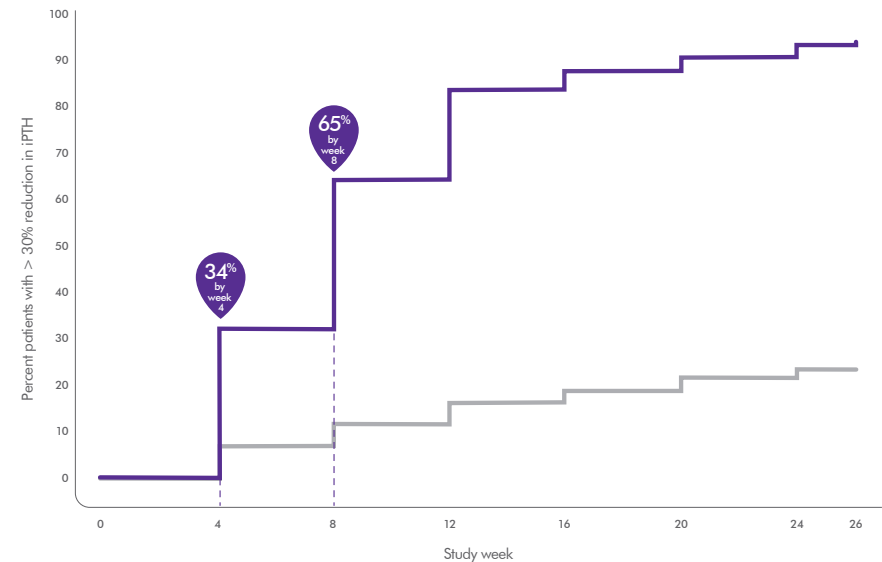
Patients with conditions that predispose to QT interval prolongation and ventricular arrhythmia may be at increased risk for QT interval prolongation and ventricular arrhythmias if they develop hypocalcemia due to Parsabiv®. Closely monitor corrected serum calcium and QT interval in patients at risk on Parsabiv®.

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One-third of patients given Parsabiv® had a reduction* in PTH by week 4—and by week 8 that number nearly doubled⁵

Post-hoc analysis: Time to first occurrence* of > 30% reduction in iPTH from combined placebo-controlled studies



■ Parsabiv® + vitamin D and/or phosphate binders† (n = 509)

■ Placebo + vitamin D and/or phosphate binders† (n = 514)

*Timepoint when > 30% reduction in iPTH was first observed.

†Vitamin D and/or phosphate binders, if prescribed.⁴

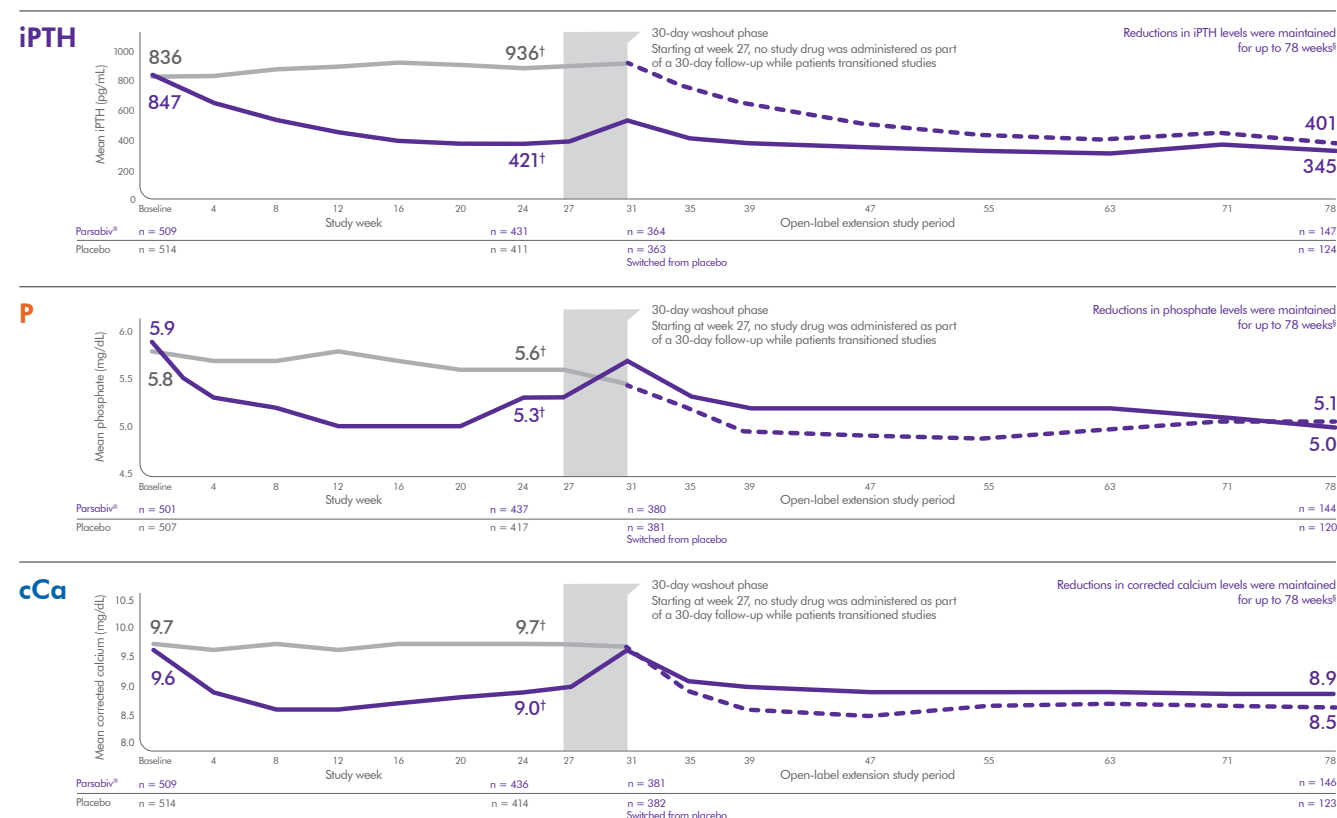
Analysis is exploratory and has not been adjusted for multiple comparisons. No conclusions of statistical or clinical significance can be drawn.

Rolling averages of 3 iPTH values (from previous, current, and next visit) were used.

- The starting dose of Parsabiv® was 5 mg three times a week (TIW) at the end of hemodialysis
- The dose was titrated at weeks 5, 9, 13, and 17 to achieve predialysis serum iPTH ≤ 300 pg/mL. The dose could be increased in 2.5 mg or 5 mg increments based on predialysis iPTH and cCa concentrations

Parsabiv® provided significant reductions across 3 key sHPT lab values vs placebo^{3,6*}

Mean iPTH, phosphate, and corrected calcium over time



*P < 0.001 (mean percent change in efficacy assessment period, defined as weeks 20 through 27).

Open-label extension: data pooled for patients receiving Parsabiv® across two placebo-controlled parent studies and a subsequent open-label extension (OLE) study, starting from the baseline of the parent study until the end or the prespecified cutoff date of the OLE study, whichever was earlier. Weeks 27 to 31 were the 30-day drug-free period (the 30-day follow-up period of the phase 3 study before entry into the extension study).² During the OLE, the starting dose of Parsabiv® for all subjects was 5 mg. The Parsabiv® dose could be increased at OLE weeks 5, 9, 17, 25, 33, 41, and 49 to a maximum dose of 15 mg to achieve predialysis serum iPTH ≤ 300 pg/mL while maintaining appropriate serum cCa concentrations. Investigators were blinded to iPTH results during the first 10 weeks of treatment. Subsequent dose adjustment was determined by the investigator per protocol guidelines.⁷

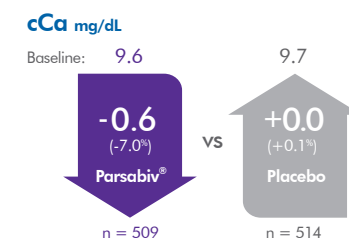
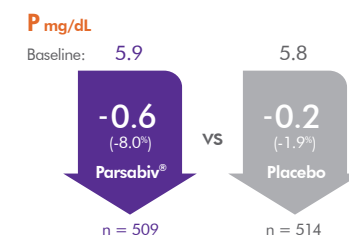
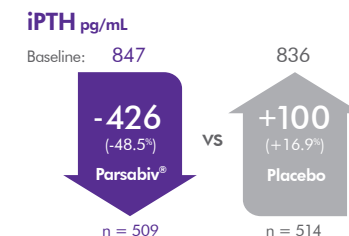
†Values represent mean iPTH during efficacy assessment phase (EAP), defined as weeks 20 through 27, inclusive.³

‡Vitamin D and/or phosphate binders, if prescribed.⁴

§Value represents iPTH measured at the first hemodialysis session in week 79.⁶

Absolute (mean % change from baseline) during EAP

P < 0.001 vs placebo



What impact does Parsabiv® have on PTH, phosphate, and corrected calcium levels?

Important Safety Information for Parsabiv®

Significant reductions in corrected serum calcium may lower the threshold for seizures. Patients with a history of seizure disorder may be at increased risk for seizures if they develop hypocalcemia due to Parsabiv®.

Please see additional Important Safety Information for Parsabiv® and Sensipar® on page 13.

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What adverse reactions were experienced in the Parsabiv® combined phase 3 studies?

Please see additional Important Safety Information for Parsabiv® and Sensipar® on page 13.

Adverse reactions reported in $\geq 5\%$ of Parsabiv®-treated patients¹

Combined placebo-controlled studies

	Parsabiv® (N = 503)	Placebo (N = 513)
Adverse Reaction*	%	%
Blood calcium decreased [†]	64	10
Muscle spasms	12	7
Diarrhea	11	9
Nausea	11	6
Vomiting	9	5
Headache	8	6
Hypocalcemia [‡]	7	0.2
Paresthesia [§]	6	1

*Included adverse reactions reported with at least 1% greater incidence in the Parsabiv® group compared to the placebo group.

[†]Asymptomatic reductions in calcium below 7.5 mg/dL or clinically significant asymptomatic reductions in corrected serum calcium between 7.5 and < 8.3 mg/dL (that required medical management).

[‡]Symptomatic reductions in corrected serum calcium < 8.3 mg/dL.

[§]Paresthesia includes preferred terms of paresthesia and hypoesthesia.

Discontinuations

- Overall, in combined placebo-controlled studies, 1.8% of patients in the Parsabiv® group and 2.5% of patients in the placebo group discontinued treatment due to an adverse event⁸

Low serum calcium

- Most events of blood calcium decrease or hypocalcemia were mild or moderate in severity in both the placebo and Parsabiv® groups^{8,9}
- In combined placebo-controlled studies, 1% of patients who received Parsabiv® discontinued treatment due to low corrected serum calcium vs 0% with placebo¹

How was the Parsabiv® vs Sensipar® (cinacalcet) head-to-head study designed?

Important Safety Information for Parsabiv®

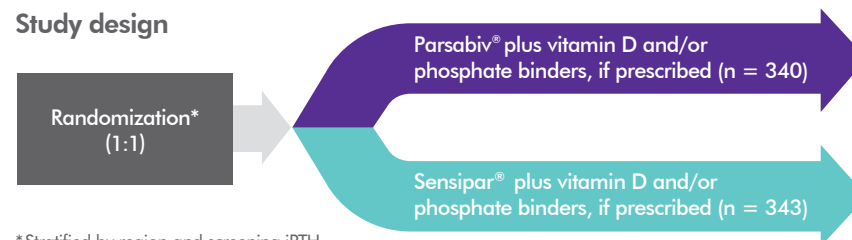
Monitor corrected serum calcium in patients with seizure disorders on Parsabiv®.

Please see additional Important Safety Information for Parsabiv® and Sensipar® on page 13.

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Parsabiv® was evaluated in a head-to-head study vs oral Sensipar® (cinacalcet) tablets^{10,11}

Study design



*Stratified by region and screening iPTH.

- A phase 3, 26-week, randomized, active-controlled, double-blind, double-dummy study comparing Parsabiv® with Sensipar® in patients with CKD on hemodialysis with iPTH > 500 pg/mL and corrected calcium $\geq$ 8.3 mg/dL (N = 683)
- Parsabiv® IV TIW + daily oral placebo vs daily oral Sensipar® + placebo IV TIW for 26 weeks
- Mean baseline iPTH in the Parsabiv® group and Sensipar® group were 1092 pg/mL and 1139 pg/mL, respectively
- The average weekly dose of investigational product during the efficacy assessment period (defined as weeks 20 through 27, inclusive) was 21 mg for Parsabiv® and 405 mg for Sensipar®
- Adherence to investigational product through 26-week study period was:
 - 97% for Parsabiv®
 - 94% for Sensipar®

Titration¹⁰

- Parsabiv® dose uptitrated from 5 mg in 2.5 mg or 5 mg increments, up to a maximum dose of 15 mg, at weeks 5, 9, 13, and 17 to target predialysis $100 \leq$ iPTH $\leq$ 300 pg/mL while maintaining cCa $\geq$ 8.3 mg/dL
- Sensipar® dose uptitrated from 30 mg daily in 30 mg increments, up to a maximum dose of 180 mg daily, at weeks 5, 9, 13, and 17 to target predialysis $100 \leq$ iPTH $\leq$ 300 pg/mL while maintaining cCa $\geq$ 8.3 mg/dL
- Parsabiv® was withheld if any of the following were observed: iPTH < 100 pg/mL (two consecutive measurements), corrected calcium < 7.5 mg/dL, symptomatic hypocalcemia, other drug-related adverse events
- Investigators were blinded to central laboratory serum iPTH values, and routine local iPTH monitoring during the study was suspended

Important Study Information

- At trial end, average Parsabiv® doses were higher than Sensipar® doses (relative to each product's respective maximally recommended dose) and a greater proportion of Parsabiv®-treated subjects achieved a maximally recommended dose
- The Parsabiv® arm had:
 - A higher relative starting dose
 - Higher relative dose increments per dose escalation steps
 - Fewer dose steps needed to reach the maximally recommended dose
- No differences in tolerability were identified to explain the lack of dose adjustment in the Sensipar® arm

How did Parsabiv® and Sensipar® (cinacalcet) reduce PTH levels?

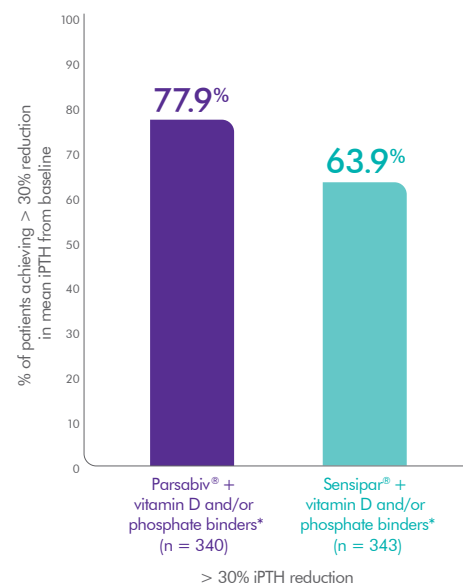
Important Safety Information for Parsabiv®

Concurrent administration of Parsabiv® with another oral calcimimetic could result in severe, life-threatening hypocalcemia. Patients switching from cinacalcet to Parsabiv® should discontinue cinacalcet for at least 7 days prior to initiating Parsabiv®. Closely monitor corrected serum calcium in patients receiving Parsabiv® and concomitant therapies known to lower serum calcium.

Please see additional Important Safety Information for Parsabiv® and Sensipar® on page 13.



Parsabiv® and Sensipar® (cinacalcet) patients who achieved a > 30% reduction from baseline in mean PTH^{10,11}



Parsabiv® was non-inferior to Sensipar® with respect to the proportion of patients who achieved a > 30% reduction from baseline in mean iPTH during the EAP (77.9% vs 63.9%; estimated treatment difference of -10.5%; 95% CI: -17.45%, -3.51%); $P < 0.001$ ^{10,11}

*Vitamin D and/or phosphate binders, if prescribed.¹⁰

Given the single, limited-duration (26-week) study design and important study information, these data should not be interpreted as providing evidence of superiority of Parsabiv® to Sensipar®. The potential impact of the difference between treatment groups on clinical outcomes has not been studied, and the clinical meaningfulness of such a difference is unknown.

Evaluating additional endpoints in the head-to-head study

Because the primary endpoint was met, the statistical analysis plan called for the sequential testing of the key secondary endpoints including mean number of days of vomiting or nausea per week in the first 8 weeks

- No statistically significant difference between the two groups was observed for the secondary endpoint evaluating the mean number of days of vomiting or nausea per week in the first 8 weeks
- Therefore, other secondary and exploratory endpoints were subsequently evaluated, but were not formally tested for statistical significance. **These endpoints included:**
 - Percent change from baseline in mean cCa during the EAP
 - Percent change from baseline in mean phosphate during EAP
 - Percent change from baseline in iPTH during EAP

EAP = efficacy assessment period.

How did Parsabiv® and Sensipar® (cinacalcet) impact PTH, phosphate, and corrected calcium levels?

Important Safety Information for Parsabiv®

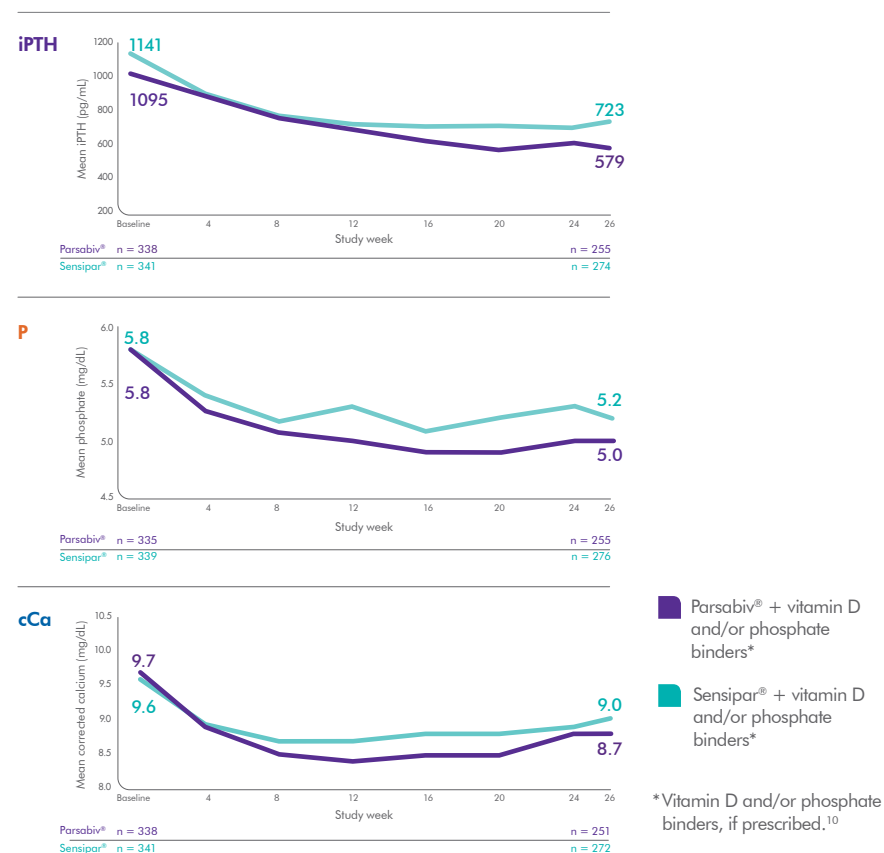
Measure corrected serum calcium prior to initiation of Parsabiv®. Do not initiate in patients if the corrected serum calcium is less than the lower limit of normal. Monitor corrected serum calcium within 1 week after initiation or dose adjustment and every 4 weeks during treatment with Parsabiv®.

Please see additional Important Safety Information for Parsabiv® and Sensipar® on page 13.

Parsabiv®
(etelcalcetide) Injection for intravenous use
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In the head-to-head study, patients given Parsabiv® achieved reductions in all 3 key sHPT labs: PTH, phosphorus, and calcium¹¹

Mean iPTH, phosphate, and corrected calcium over time



Analysis is exploratory and has not been adjusted for multiple comparisons. No conclusions of statistical or clinical significance can be drawn.

Given the single, limited-duration (26-week) study design and important study information, these data should not be interpreted as providing evidence of superiority of Parsabiv® to Sensipar®. The potential impact of the difference between treatment groups on clinical outcomes has not been studied, and the clinical meaningfulness of such a difference is unknown.

How did patients' starting PTH levels impact PTH reductions with Parsabiv®?

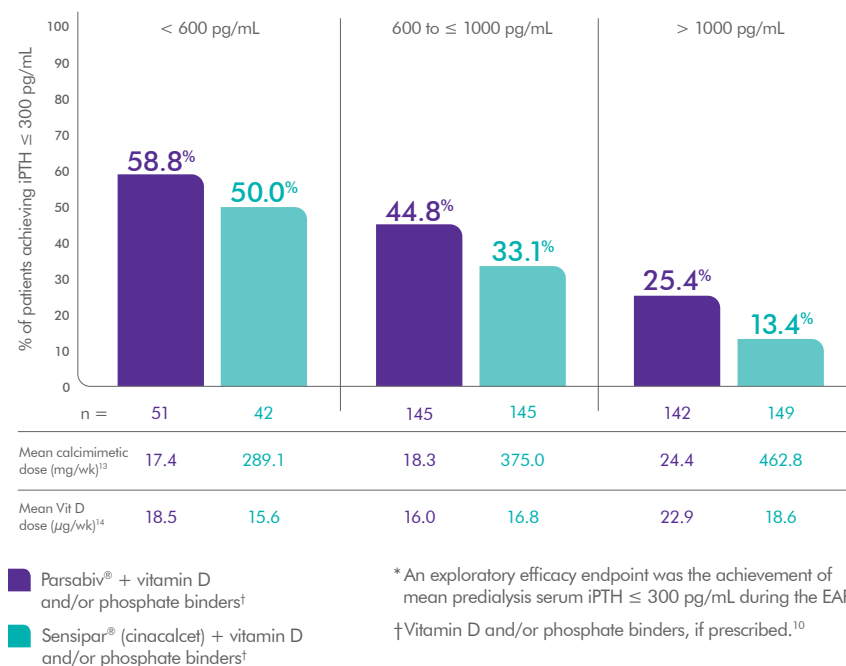
Important Safety Information for Parsabiv®

Measure PTH 4 weeks after initiation or dose adjustment of Parsabiv®. Once the maintenance dose has been established, measure PTH per clinical practice.

Please see additional Important Safety Information for Parsabiv® and Sensipar® on page 13.

In the head-to-head study, 6 out of 10 patients achieved PTH treatment goal* when Parsabiv® was initiated at PTH < 600 pg/mL¹²

Subgroup analysis: Patients achieving study iPTH treatment goal during EAP by screening iPTH



In an exploratory analysis of the head-to-head study, 38.5% of all Parsabiv® patients achieved iPTH ≤ 300 pg/mL vs 26.2% of all Sensipar® patients during the Efficacy Assessment Phase.

Analysis is exploratory and has not been adjusted for multiple comparisons. No conclusions of statistical or clinical significance can be drawn.

What adverse events were experienced in the head-to-head study?

Please see additional Important Safety Information for Parsabiv® and Sensipar® on page 13.

Treatment-emergent adverse events experienced by $\geq 5\%$ of Parsabiv® - or Sensipar® (cinacalcet)-treated patients^{10,11}

Head-to-head study (active-controlled)

	Parsabiv® (n = 338)	Sensipar® (n = 341)
Treatment Emergent Adverse Events*	%	%
Blood calcium decreased†	69	60
Nausea	18	23
Vomiting	13	14
Hypotension	7	3
Headache	7	7
Muscle spasms	7	6
Diarrhea	6	10
Hypertension	6	7
Anemia	5	4
Hypocalcemia	5	2
Pain in extremity	5	4
Bronchitis	2	5

*The term treatment emergent refers to a condition either not present before exposure to a study drug that develops after drug exposure or a condition present before exposure that worsens in frequency or severity. Adverse events occurring after the first dose of study drug and up to 30 days after the last dose of study drug were included. Counts and proportions refer to patients rather than to adverse events. In other words, patients may have one or more adverse event.

†Defined as an albumin-corrected serum calcium concentration lower than 8.3 mg/dL (to convert to mmol/L, multiply by 0.25) that resulted in a medical intervention.

Indications and Important Safety Information for Parsabiv® (etelcalcetide) and Sensipar® (cinacalcet)

Indications

Parsabiv® (etelcalcetide) is indicated for the treatment of secondary hyperparathyroidism (HPT) in adult patients with chronic kidney disease (CKD) on hemodialysis.

Sensipar® (cinacalcet) is indicated for the treatment of secondary HPT in adult patients with CKD on dialysis.

Limitations of Use:

Parsabiv® has not been studied in adult patients with parathyroid carcinoma, primary hyperparathyroidism, or with CKD who are not on hemodialysis and is not recommended for use in these populations.

Sensipar® is not indicated for use in patients with CKD who are not on dialysis because of an increased risk of hypocalcemia.

Important Safety Information

Contraindications: Parsabiv® (etelcalcetide) is contraindicated in patients with known hypersensitivity to etelcalcetide or any of its excipients. Hypersensitivity reactions, including face edema and anaphylactic reaction, have occurred.

Sensipar® (cinacalcet) treatment initiation is contraindicated if serum calcium is less than the lower limit of the normal range (8.4 mg/dL).

Hypocalcemia: Parsabiv® and Sensipar® lower serum calcium and can lead to hypocalcemia, sometimes severe. Life threatening events and fatal outcomes associated with hypocalcemia have been reported in patients treated with Sensipar®, including pediatric patients. The safety and effectiveness of Sensipar® have not been established in pediatric patients.

Significant lowering of serum calcium can cause QT interval prolongation and ventricular arrhythmia. Cases of QT prolongation and ventricular arrhythmia have been reported in patients treated with Sensipar®. Patients with 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 Parsabiv® or Sensipar®. Closely monitor corrected serum calcium and QT interval in patients at risk on Parsabiv® or Sensipar®.

Significant reductions in corrected serum calcium may lower the threshold for seizures. Patients with a history of seizure disorder may be at increased risk for seizures if they develop hypocalcemia due to Parsabiv® or Sensipar®. Monitor corrected serum calcium in patients with seizure disorders on Parsabiv® or Sensipar®.

Concurrent administration of Parsabiv® or Sensipar® with calcium-lowering drugs including other calcimimetics could result in severe, life-threatening hypocalcemia. Parsabiv® and Sensipar® should not be given together. Patients switching from Sensipar® to Parsabiv® should discontinue Sensipar® for at least 7 days prior to initiating Parsabiv®. Closely monitor corrected serum calcium in patients receiving Parsabiv® or Sensipar® and concomitant therapies known to lower serum calcium.

Measure corrected serum calcium prior to initiation of Parsabiv®. Do not initiate in patients if the corrected serum calcium is less than the lower limit of normal. Monitor corrected serum calcium within 1 week after initiation or dose adjustment and every 4 weeks during treatment with Parsabiv®. Measure PTH 4 weeks after initiation or dose adjustment of Parsabiv®. Once the maintenance dose has been established, measure PTH per clinical practice.

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®. Once the maintenance dose has been established, serum calcium and serum phosphorus should be measured approximately monthly, and PTH every 1 to 3 months.

Hypotension, Worsening Heart Failure and/or Arrhythmias: In Parsabiv® clinical studies, cases of hypotension, congestive heart failure, and decreased myocardial performance have been reported. Closely monitor patients treated with Parsabiv® for worsening signs and symptoms of heart failure.

In Sensipar® 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® therapy could not be completely excluded and may be mediated by reductions in serum calcium levels.

Upper Gastrointestinal Bleeding: Cases of gastrointestinal (GI) bleeding, mostly upper GI bleeding, have occurred in patients using calcimimetics, including Sensipar®, from postmarketing and clinical trial sources.

In clinical studies, 2 patients treated with Parsabiv® in 1253 patient years of exposure had upper GI bleeding at the time of death. There were too few cases to determine whether these cases were related to Parsabiv®.

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 with Parsabiv® or Sensipar®. Monitor patients for worsening of common Parsabiv® or Sensipar® GI adverse reactions and for signs and symptoms of GI bleeding and ulcerations during Parsabiv® or Sensipar® therapy.

Adynamic Bone: Adynamic bone may develop if PTH levels are chronically suppressed.

Adverse Reactions: In clinical trials of patients with secondary HPT comparing Parsabiv® to placebo, the most common adverse reactions were blood calcium decreased (64% vs. 10%), muscle spasms (12% vs. 7%), diarrhea (11% vs. 9%), nausea (11% vs. 6%), vomiting (9% vs. 5%), headache (8% vs. 6%), hypocalcemia (7% vs. 0.2%), and paresthesia (6% vs. 1%).

In clinical trials of patients with secondary HPT comparing Sensipar® to placebo, the most commonly reported side effects were nausea (31% vs. 19%), vomiting (27% vs. 15%), and diarrhea (21% vs. 20%).

[Please click here to see accompanying Parsabiv® full Prescribing Information.](#)

[Please click here to see accompanying Sensipar® full Prescribing Information.](#)

What should I know before initiating patients on Parsabiv®?

Important Safety Information for Parsabiv®

In Parsabiv® clinical studies, cases of hypotension, congestive heart failure, and decreased myocardial performance have been reported. Closely monitor patients treated with Parsabiv® for worsening signs and symptoms of heart failure.

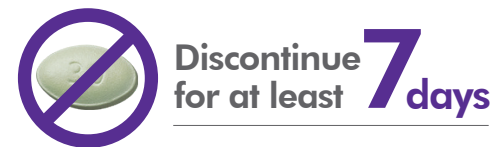
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Before you initiate Parsabiv®

Switching to Parsabiv® from oral cinacalcet

Ensure your patient discontinues use of oral cinacalcet for at least 7 days prior to starting Parsabiv®¹



- Initiate Parsabiv® after day 7, if corrected serum calcium is at or above the lower limit of normal*

The approved starting dose

Initiate Parsabiv® at 5 mg, 3 times per week¹

5 mg starting dose	3x a week	During rinse back or IV after rinse back
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- Do not administer Parsabiv® more frequently than 3 times per week¹
- Ensure corrected serum calcium is at or above the lower limit of normal prior to Parsabiv® initiation, a dose increase, or reinitiation after dosing interruption¹
- If a regularly scheduled hemodialysis treatment is missed, DO NOT administer any missed doses. Resume Parsabiv® at the end of the next hemodialysis treatment at the prescribed dose¹
- If doses of Parsabiv® are missed for more than 2 weeks, reinitiate Parsabiv® at the recommended starting dose of 5 mg (or 2.5 mg if that was the patient's last dose)¹

*Lower limit of reference range in phase 3 trials was 8.3 mg/dL.^{1,4}

What might I see when switching patients from higher doses of oral cinacalcet to Parsabiv®?

Important Safety Information for Parsabiv®

In clinical studies, 2 patients treated with Parsabiv® in 1253 patient years of exposure had upper gastrointestinal (GI) bleeding at the time of death. The exact cause of GI bleeding in these patients is unknown and there were too few cases to determine whether these cases were related to Parsabiv®.

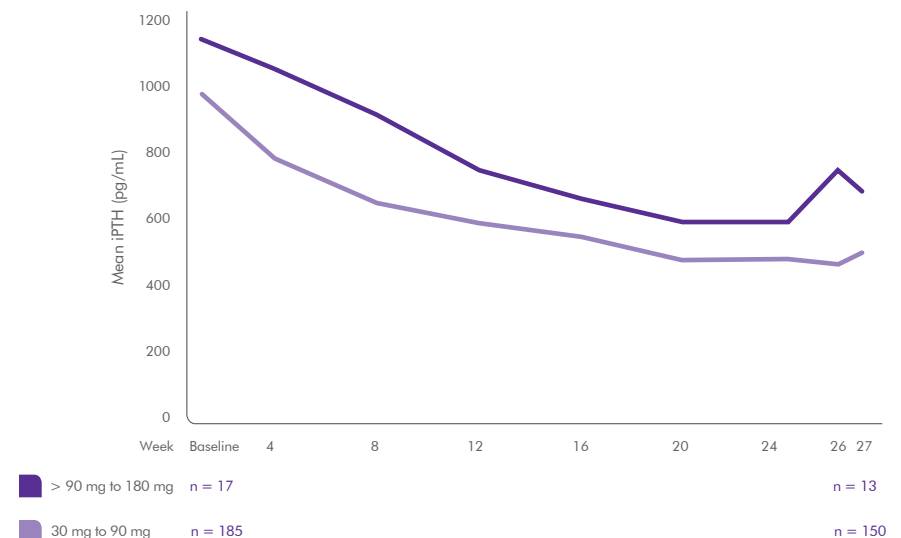
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When switching to Parsabiv®, consider prior oral cinacalcet dose when evaluating early results

In a post-hoc analysis, phase 3 trials showed that when initiating Parsabiv® 5 mg three times weekly after a minimum 7-day washout of oral cinacalcet, results correlated with previous oral cinacalcet dose strength¹⁵

Mean iPTH by prior oral cinacalcet dose¹⁵



Total placebo-controlled studies: Studies 20120229 and 20120230. Based on exclusion criteria, patients were required to be off oral cinacalcet at least 4 weeks before entering trial. Only oral cinacalcet records with stop date prior to and within one year of treatment start date are considered. The last oral cinacalcet dose prior to the treatment start date is used in the analysis.

Analysis is exploratory and has not been adjusted for multiple comparisons. No conclusions of statistical or clinical significance can be drawn.

Parsabiv® was titrated no more frequently than every 4 weeks to a maximum dose of 15 mg three times a week to achieve target PTH^{4,16,17}

- The starting dose of Parsabiv® was 5 mg at the end of hemodialysis three times per week^{4,16,17}
- The dose was titrated by 2.5 mg or 5 mg at weeks 5, 9, 13, and 17 to achieve predialysis serum iPTH ≤ 300 pg/mL^{4,16,17}
- The average dose of Parsabiv® at the time of the efficacy assessment period (defined as weeks 20 through 27, inclusive) was 7.2 mg three times a week¹

How do I monitor and titrate Parsabiv®?

Parsabiv® is available in 3 different, single-use, single-dose vials¹

Vials shown are not actual size.



Important Safety Information for Parsabiv®

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 with Parsabiv®. Monitor patients for worsening of common Parsabiv® GI adverse reactions and for signs and symptoms of GI bleeding and ulcerations during Parsabiv® therapy.

Please see additional Important Safety Information for Parsabiv® and Sensipar® on page 13.

Parsabiv®
(etelcalcetide) Injection for intravenous use
2.5mg/0.5mL | 5mg/1mL | 10mg/2mL

How to monitor and titrate Parsabiv®

Check their labs and know where they stand¹

	PTH	Corrected Serum Calcium
Lab measurements after initiation or dose adjustment	after 4 weeks	at 1 week
Lab measurements once maintenance dose is established	per clinical practice	every 4 weeks

Adjust dose based on PTH and corrected serum calcium¹

Start at 5 mg—then titrate up or down

Reductions too great? Titrate down:

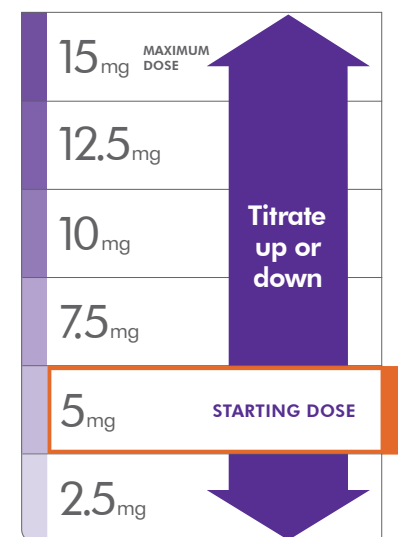
- Decrease or temporarily discontinue Parsabiv® when PTH is below target range
- Consider decreasing or temporarily discontinuing Parsabiv®, or use concomitant therapies,* when corrected serum calcium is below lower limit of normal† but ≥ 7.5 mg/dL without symptoms of hypocalcemia

Need greater reductions? Titrate up:

- Increase the dose of Parsabiv® in 2.5 mg or 5 mg increments until PTH is within recommended target range and corrected serum calcium is within normal range
- Increase no more frequently than every 4 weeks up to a maximum dose of 15 mg three times per week

Reinitiating Parsabiv®:

- If dose is stopped, reinitiate Parsabiv® at a lower dose when PTH is within target range and hypocalcemia has been corrected



* Concomitant therapies include calcium, calcium-containing phosphate binders, and/or vitamin D sterols or increases in dialysate calcium concentration.

† Lower limit of reference range in phase 3 trials was 8.3 mg/dL.^{1,10}

How do I manage calcium levels in patients on Parsabiv®?

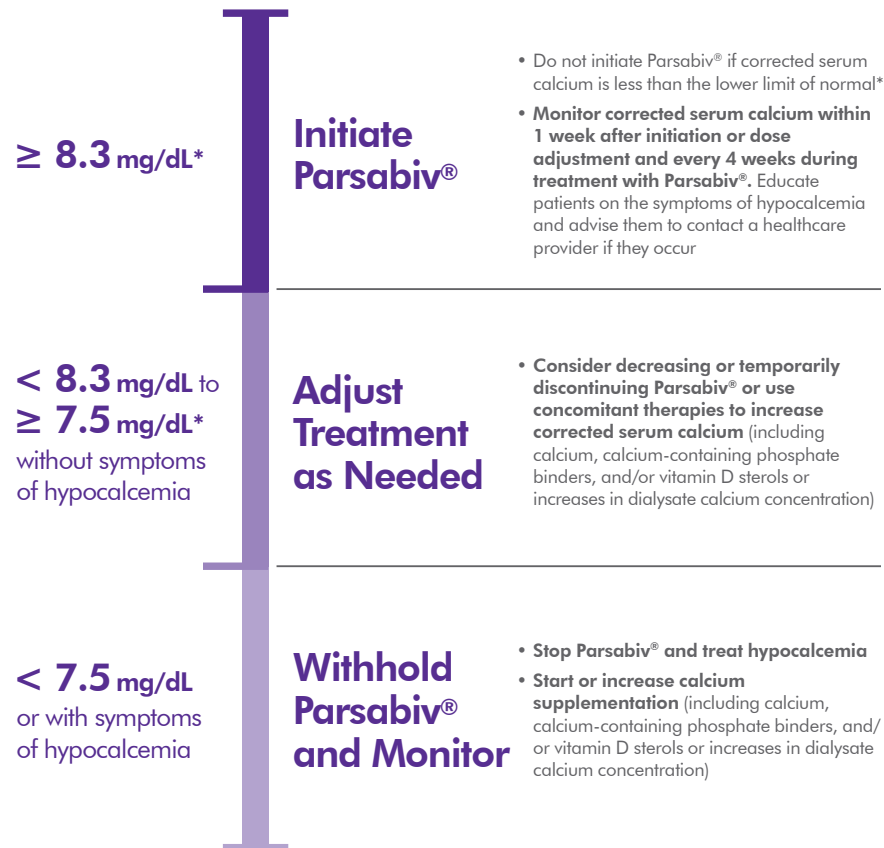
Important Safety Information for Parsabiv®

Adynamic bone may develop if PTH levels are chronically suppressed.

Please see additional Important Safety Information for Parsabiv® and Sensipar® on page 13.

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Managing calcium in patients taking Parsabiv®¹



- Throughout the studies, dialysate calcium concentration could be adjusted but had to remain ≥ 2.25 mEq/L¹
- Significant lowering of serum calcium can cause paresthesias, myalgias, muscle spasms, seizures, QT interval prolongation, and ventricular arrhythmias¹

*Lower limit of reference range in phase 3 trials was 8.3 mg/dL.^{1,4}

When cCa returns ≥ 8.3 mg/dL* — Reinitiate Parsabiv®

- When corrected serum calcium levels are within normal limits, symptoms of hypocalcemia have resolved, and predisposing factors for hypocalcemia have been addressed, reinitiate Parsabiv® at a dose 5 mg lower than the last administered dose. If patient's last administered dose of Parsabiv® was 2.5 mg or 5 mg, reinitiate at a dose of 2.5 mg

How did calcium reductions correspond with patients' baseline corrected calcium levels?

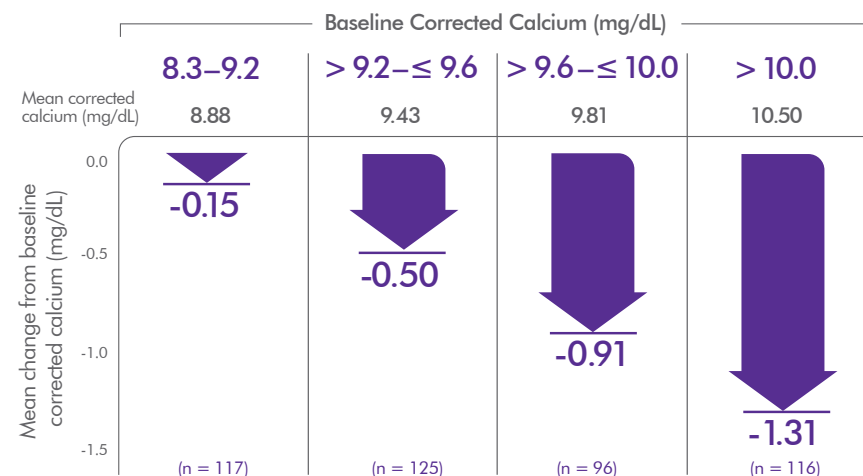
Important Safety Information for Parsabiv®

In clinical trials of patients with secondary HPT comparing Parsabiv® to placebo, the most common adverse reactions were blood calcium decreased (64% vs. 10%), muscle spasms (12% vs. 7%), diarrhea (11% vs. 9%), nausea (11% vs. 6%), vomiting (9% vs. 5%), headache (8% vs. 6%), hypocalcemia (7% vs. 0.2%), and paresthesia (6% vs. 1%).

Please see additional Important Safety Information for Parsabiv® and Sensipar® on page 13.

Calcium reductions by baseline corrected calcium level

In combined placebo-controlled studies, calcium reductions with Parsabiv® during the efficacy assessment period were lowest among patients initiated at the lowest baseline calcium (8.3-9.2 mg/dL)¹⁸



Regardless of baseline calcium, levels remained above the lower limit of normal^{18*}

Post-hoc analysis of pooled data from two phase 3, 26-week, randomized, double-blind, placebo-controlled studies comparing Parsabiv® with placebo in patients with CKD on hemodialysis with iPTH > 400 pg/mL and corrected calcium ≥ 8.3 mg/dL (N = 1023). Patients in both treatment arms could be treated with vitamin D sterols and/or phosphate binders. Mean baseline iPTH in the Parsabiv® group and placebo group were 847 pg/mL and 836 pg/mL, respectively. The primary endpoint of each study was the proportion of patients who achieved a > 30% reduction from baseline in mean iPTH during the efficacy assessment period (defined as weeks 20 through 27, inclusive).^{1,3,4}

Data are presented by baseline corrected calcium quartile for Parsabiv®-treated patients only.¹⁸

*Lower limit of reference range in phase 3 trials was 8.3 mg/dL.^{1,4}

References

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