Parsabiv® (Etelcalcetide)

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Community Plan Policy

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Coverage Rationale

Initial Therapy

Parsabiv (etelcalcetide) is proven for the treatment of secondary hyperparathyroidism with chronic kidney disease when the following criteria are met:

- Diagnosis of secondary hyperparathyroidism with chronic kidney disease; **and**
- Patient is on dialysis; **and**
- Patient is not receiving Parsabiv (etelcalcetide) in combination with Sensipar (cinacalcet hydrochloride); **and**
- Prescribed by or in consultation with an endocrinologist or nephrologist; **and**
- Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Initial authorization will be for no longer than 12 months.

Parsabiv (etelcalcetide) is medically necessary for the treatment of secondary hyperparathyroidism with chronic kidney disease when the following criteria are met:

- Diagnosis of secondary hyperparathyroidism with chronic kidney disease; **and**
- Patient is on dialysis; **and**
- **All** of the following:
  - History of failure, contraindication, or intolerance to **one** phosphate binder (e.g., PhosLo, Fosrenol, Renvela, Renagel, etc.); **and**
  - History of failure, contraindication, or intolerance to **one** vitamin D analog (e.g., calcitriol, Hectorol, Zemplar, etc.); **and**
  - History of failure of maximum tolerated dosage, adverse reaction, or contradiction to Sensipar (cinacalcet hydrochloride)

  and
- Patient is not receiving Parsabiv (etelcalcetide) in combination with Sensipar (cinacalcet hydrochloride); **and**
- Prescribed by or in consultation with an endocrinologist or nephrologist; **and**
- Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Initial authorization will be for no longer than 12 months.

Continuation Therapy

Parsabiv (etelcalcetide) will be reauthorized based on all of the following criteria:

- Documentation of a reduction in serum calcium from baseline; **and**
- Patient is not receiving Parsabiv (etelcalcetide) in combination with Sensipar (cinacalcet hydrochloride); **and**
- Prescribed by or in consultation with an endocrinologist or nephrologist; **and**

- Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Reauthorization will be for no longer than 12 months.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J0606	Injection, etelcalcetide, 0.1 mg

Background

Parsabiv is a calcimimetic agent that allosterically modulates the calcium-sensing receptor (CaSR). Etelcalcetide binds to the CaSR and enhances activation of the receptor by extracellular calcium. Activation of the CaSR on parathyroid chief cells decreases PTH secretion.[1]

Clinical Evidence

In 2 parallel, phase 3, randomized, placebo-controlled treatment trials, Block et al evaluated the effect of the etelcalcetide on serum parathyroid hormone (PTH) concentrations in patients receiving hemodialysis.[3] Study participants received etelcalcetide or placebo after each hemodialysis session for 26 weeks. The primary end point was the proportion of patients achieving greater than 30% reduction in mean PTH over baseline during weeks 20-27, while the secondary end point was the proportion of patients reaching a mean PTH of 300 pg/mL or lower. Patients randomized to etelcalcetide were significantly more likely to achieve the primary and secondary endpoints. Regarding adverse events for both trials, patients receiving etelcalcetide had more muscle spasms, as well as nausea and vomiting. The authors conclude that in patients receiving hemodialysis with moderate to severe secondary hyperparathyroidism, use of etelcalcetide vs. placebo resulted in greater reduction in serum PTH over 26 weeks.

Block GA et al evaluated the therapeutic efficacy and safety of IV etelcalcetide and oral cinacalcet in patients receiving hemodialysis with moderate to severe secondary hyperparathyroidism in a randomized, active control, double-blind phase 3 trial.[2] The trial compared IV etelcalcetide vs. oral placebo and oral cinacalcet vs. IV placebo in 683 patients receiving hemodialysis with serum parathyroid hormone (PTH) concentrations higher than 500 pg/mL on therapy. The patients received either etelcalcetide intravenously with oral placebo or oral cinacalcet with IV placebo for 26 weeks. Administration of the IV formulation was administered 3 times weekly with hemodialysis, while the oral formulation was administered daily. The primary end point was noninferiority of etelcalcetide at achieving more than a 30% reduction in mean predialysis PTH concentrations from baseline during weeks 20-27. Secondary end points included superiority in achieving biochemical end points (> 50% and > 30% reduction in PTH) as well as self-reported nausea or vomiting. Etelcalcetide was noninferior to cinacalcet on the primary end point. The estimated difference in proportions of patients achieving reduction in PTH concentrations of more than 30% between the 198 of 343 patients (57.7%) randomized to receive cinacalcet and the 232 of 340 patients (68.2%) randomized to receive etelcalcetide was -10.5%(95%CI, -17.5% to -3.5%, P for noninferiority, < .001; P for superiority, .004). One hundred seventy-eight patients (52.4%) to randomized etelcalcetide achieved more than 50% reduction in PTH concentrations compared with 138 patients (40.2%) randomized to cinacalcet (P = .001; difference in proportions, 12.2%; 95%CI, 4.7%to 19.5%). The most common adverse effect was decreased blood calcium (68.9%vs 59.8%). The authors conclude that patients with moderate to severe secondary hyperparathyroidism receiving hemodialysis, the use of etelcalcetide was not inferior to, and met superiority criteria when compare to cinacalcet. The authors state that additional studies are needed to determine clinical outcomes in addition to efficacy and safety beyond the study period.

Professional Societies

In 2017, Kidney Disease: Improving Global Outcomes (KDIGO) published an update to their 2009 Clinical Practice Guidelines for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic kidney disease – Mineral and Bone Disorder (CKD-MBD).[4] Recommendations for the treatment of abnormal parathyroid levels in CKD-MBD are summarized below:

- In patients with CKD G3a–G5 not on dialysis, the optimal PTH level is not known. The Work Group suggests that patients with levels of intact PTH progressively rising or persistently above the upper normal limit for the assay be evaluated for modifiable factors, including hyperphosphatemia, hypocalcemia, high phosphate intake, and vitamin D deficiency (Grade 2C recommendation).
- In adult patients with CKD G3a–G5 not on dialysis, the Work Group suggests calcitriol and vitamin D analogs not be routinely used (2C). It is reasonable to reserve the use of calcitriol and vitamin D analogs for patients with CKD G4–G5 with severe and progressive hyperparathyroidism (Not Graded).
- In patients with CKD G5D requiring PTH-lowering therapy, the Work Group suggests calcimimetics, calcitriol, or vitamin D analogs, or a combination of calcimimetics with calcitriol or vitamin D analogs (Grade 2B recommendation). Calcimimetics, calcitriol, or vitamin D analogs are all acceptable first-line options in G5D patients.
- In patients with CKD G3a–G5D with severe hyperparathyroidism who fail to respond to medical or pharmacological therapy, we suggest parathyroidectomy (Grade 2B recommendation).

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Parsabiv is a calcium-sensing receptor agonist indicated for secondary hyperparathyroidism (HPT) in adult patients with chronic kidney disease (CKD) on hemodialysis.[1]

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.[1]

For patients changing from cinacalcet to Parsabiv: Discontinue cinacalcet for at least 7 days prior to starting Parsabiv, and initiate Parsabiv treatment at a starting dose of 5 mg. Ensure corrected serum calcium is at or above the lower limit of normal prior to Parsabiv initiation.[1]

References

1. Parsabiv [prescribing information]. Thousand Oaks, CA; Amgen/KAI Pharmaceuticals; February 2021.
2. Block GA, Bushinsky DA, Cheng S, Cunningham J, Dehmel B, Drueke TB, Ketteler M, Kewalramani R, Martin KJ, Moe SM, Patel UD, Silver J, Sun Y, Wang H, Chertow GM. Effect of Etelcalcetide vs Cinacalcet on Serum Parathyroid Hormone in Patients Receiving Hemodialysis With Secondary Hyperparathyroidism: A Randomized Clinical Trial. JAMA. 2017 Jan 10;317(2):156-164. doi: 10.1001/jama.2016.19468.
3. Block GA, Bushinsky DA, Cunningham J, et al. Effect of etelcalcetide on serum parathyroid hormone in patients receiving hemodialysis with secondary hyperparathyroidism: two randomized clinical trials. JAMA. doi:10.1001/jama.2016.19456.
4. Ketteler M, Block GA, Evenepoel P, et al. Executive summary of the 2017 KDIGO Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD) Guideline Update: what's changed and why it matters [published correction appears in Kidney Int. 2017 Dec;92(6):1558]. *Kidney Int*. 2017;92(1):26-36. doi:10.1016/j.kint.2017.04.006.

Policy History/Revision Information

Date	Summary of Changes
12/01/2024	**Template Update** • Modified font style; no change to policy content
04/01/2024	• Routine review; no content changes • Archived previous policy version 2023D0075G

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.