palopegteriparatide (Yorvipath®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO317

Description

Palopegteriparatide (Yorvipath) is a subcutaneously administered parathyroid hormone analog prodrug that acts as continuous endogenous parathyroid hormone (1-34) to regulate calcium and phosphate homeostasis.

Length of Authorization

- Initial: 12 months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
palopegteriparatide (Yorvipath)	Hypoparathyroidism	168 mcg/0.56 mL pen	1.12 mL/28 days (2 pens/28 days)
		294 mcg/0.98 mL pen	1.96 mL/28 days (2 pens/28 days)
		420 mcg/1.40 mL pen	2.80 mL/28 days (2 pens/28 days)

Initial Evaluation

I. **Palopegteriparatide (Yorvipath)** may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, an endocrinologist or nephrologist; **AND**
   C. A diagnosis of **hypoparathyroidism** when the following are met:
      1. The disease is present for at least 6 months; **AND**
      2. Provider attestation of normal serum vitamin D levels at baseline; **AND**
      3. Provider attestation of inappropriately low serum parathyroid hormone (PTH) levels; **AND**
      4. History of persistent hypocalcemia and a current calcium level of:
         i. Albumin-adjusted serum calcium level of 7.8 mg/dL or greater; **OR**
         ii. Ionized serum calcium level of 4.4 mg/dL or greater; **AND**
      5. The member does not have acute post-surgical hypoparathyroidism; **AND**
   D. Documentation that the member has not achieved disease control with conventional therapies of vitamin D (active: 0.25-3µg/day of calcitriol; analog: 1,000-100,000 IU per day

of cholecalciferol [D3]; 50,000 IU weekly to daily of ergocalciferol [D2]) and therapeutic doses of elemental calcium (>600mg/day); **AND**

1. The member will continue conventional therapies (active or analog vitamin D and oral calcium) in combination with palopegteriparatide (Yorvipath) unless they are contraindicated or not tolerated.

II. Palopegteriparatide (Yorvipath) is considered investigational when used for all other conditions, including but not limited to:
   A. Osteoporosis
   B. Acute post-surgical hypoparathyroidism

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has exhibited improvement or stability of disease symptoms [e.g., decrease weakness or fatigue, reduction of muscle aches or cramps] **AND**
IV. Documentation of improved albumin-corrected or ionized serum calcium into the normal reference range (albumin-corrected: 8.5 – 10.5 mg/dL; ionized serum: 4.5 – 5.6 mg/dL); **AND**
V. The member no longer requires active or analog vitamin D or therapeutic doses of elemental calcium; **OR**
   A. The member has shown significant reduction in doses of conventional therapy (active or analog vitamin D and oral calcium); **OR**
   B. The member is still titrating palopegteriparatide (Yorvipath).

Supporting Evidence

I. Palopegteriparatide (Yorvipath) was approved based on a Phase 3, randomized, double-blind, placebo-controlled (PaTHway) trial in adult patients with confirmed chronic hypoparathyroidism who were treated with conventional therapy (CT, oral calcium supplementation and active or analog vitamin D products). Patients received either palopegteriparatide (Yorvipath) or placebo while continuing CT. The starting dose of palopegteriparatide (Yorvipath) was 18 mcg once daily and titrated to an optimal dose per protocol. The primary outcome was assessed at week 26 with a composite endpoint of proportion of participants who achieved albumin-adjusted serum calcium in the normal range, independence from active vitamin D and therapeutic doses of elemental calcium, and no dose increases of study drug during the 4 weeks leading up to week 26. Secondary outcomes included measurement of routine laboratory values and patient

reported outcomes (PRO) included the hypoparathyroidism patient experience scale (HPES) and short form 36 (SF-36) that evaluated quality of life and physical functioning at baseline and week 26.

II. A key inclusion criterion of the PaThway clinical trial required participants to be 18 years of age or older. The study did not contain any patients younger than 18 years and the safety and efficacy in the pediatric and adolescent population is unknown.

III. A key inclusion criteria of the PaThway clinical trial was an albumin-adjusted (≥7.8mg/dL) or ionized (≥4.4mg/dL) serum calcium within normal or slightly below normal range. Treatment in members below these cutoffs is not clinically appropriate due to being classified as having severe hypocalcemia. The safety and efficacy of palopegteriparatide (Yorvipath) has not been established in this patient population is considered a limitation for use, as the product information titration scheme was only evaluated in adults who first achieved albumin-corrected serum calcium of at least 7.8mg/dL using calcium and active vitamin D treatment.

IV. Treatment with palopegteriparatide (Yorvipath) was found to be statistically significant ($p<0.0001$) in meeting the composite endpoint at week 26 versus placebo with 48 (79%) patients in the treatment group meeting all the components of the composite endpoint against one (5%) patient in the placebo group. The PRO HPES and SF-36 showed improvement in all domains of each scale at week 26 as compared to baseline.

V. The 52-week open label extension (OLE) results showed that the primary composite endpoint was met in 81% of total participants. There was a modest percent increase of participants that met the primary endpoint but supports the ongoing durability and effect of this treatment.

VI. Injection site reactions (31% vs. 0), hypercalcemia (10% vs. 0%), and headache (21% vs. 10%) were the most reported adverse events for palopegteriparatide (Yorvipath) and placebo, respectively at week 26. There was one reported death across both groups in which a patient in the palopegteriparatide (Yorvipath) arm with multiple cardiovascular risk factors including hypertension, hyperlipidemia, and obesity who suffered a fatal cardiac arrest, but was not deemed related to the drug. There are no specific contraindications; however, warning and precautions include: hypercalcemia, hypocalcemia, unintended serum calcium changes, orthostatic hypotension, and potential risk of osteosarcoma.

VII. The 2022 Summary Statement and Guidelines for the Evaluation and Management of Hypoparathyroidism defines diagnosis of hypoparathyroidism as marked hypocalcemia in the presence of undetectable, low or inappropriately normal intact PTH level on two occasions at least two weeks apart. The guidelines do not specify a target PTH level to indicate permanent hypoparathyroidism but suggest that levels <10 pg/mL 12-24 hours post-surgery are at risk. Additional laboratory abnormalities that can arise include elevated serum phosphate, reduction in vitamin D and increase in urine calcium excretion.

VIII. Diagnosis and treatment of hypoparathyroidism is highly specialized. To ensure an appropriate diagnosis and that the benefits of treatment outweigh the risks, prescribing by, or in consultation with, an endocrine or nephrology specialist is required.

IX. About 70-80% of patients with post-surgery parathyroid failure will recover within a month and therapy can be weaned. Chronic disease is defined as no adequate control of calcium and vitamin D levels despite CT for at least 6 months.

X. The most common cause of hypoparathyroidism is related to removal or damage to the parathyroid glands during thyroid-related surgery. Symptoms and other complications can include cataracts, renal calcification, neurological manifestations and cardiac abnormalities. Conventional therapy is intended to treat hypocalcemia with therapeutic doses of elemental calcium (>600mg/day) and active (0.25-3µg/day of calcitriol) or analog (1,000-100,000 IU per day of cholecalciferol [D3]; 50,000 IU weekly to daily of ergocalciferol [D2]) forms of vitamin D above the daily recommended levels. Additional agents such as thiazide diuretics, magnesium supplementation, and phosphate binders can be considered in specific scenarios.

XI. The guidelines suggest if disease control is unattainable despite treatment with conventional therapy, that parathyroid hormone (PTH) replacement can be considered. Inadequate disease control despite conventional therapy is presented as fluctuation of calcium levels, hyperphosphatemia, renal impairment or other renal-related disease or issues. Other considerations include compliance with therapy, malabsorption or GI side effects. Parathyroid hormone (Natpara) was approved in 2015 as an adjunct treatment along with conventional therapy for hypoparathyroid-related hypocalcemia. In 2019, the manufacturer initiated a product recall due to production issues and they indicated that it would stop all production by the end of 2024, including the special use program. The guideline does mention use of palopegteriparatide (Yorvipath) but was not FDA approved at the time of publication.

Investigational or Not Medically Necessary Uses

I. Palopegteriparatide (Yorvipath) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Osteoporosis
      i. Palopegteriparatide (Yorvipath) is a prodrug analog of inert teriparatide. Teriparatide under brand name (Forteo) and generics is FDA-approved for treatment of osteoporosis. In the 52-week OLE results showed improvements to bone health related values (bone mineral density [BMD] and type 1 N-terminal propeptide [P1NP]). However, the improvements were minor and would not provide an adequate response if primarily used as an osteoporosis treatment. As of November 2024, the manufacturer confirmed that they are not actively pursuing approval in this space.
   B. Acute post-surgical hypoparathyroidism
      i. Palopegteriparatide (Yorvipath) was not studied in acute postsurgical hypoparathyroidism. Guidelines indicate that post-surgical PTH levels <10 pg/mL 12-24 hours could be an indication of permanent hypoparathyroidism, the risk is

less than 50%. Additionally, 70-80% of individuals will likely recover within a month on conventional therapy, at which point can be gradually withdrawn.

References

1. Yorvipath. Package Insert. Ascendis Pharma; August 2024.
2. Khan AA, Bilezikian JP, Brandi ML, et al. Evaluation and Management of Hypoparathyroidism Summary Statement and Guidelines from the Second International Workshop. J Bone Miner Res. 2022;37(12):2568-2585. doi:10.1002/jbmr.4691
3. Khan AA, Rubin MR, Schwarz P, et al. Efficacy and Safety of Parathyroid Hormone Replacement With TransCon PTH in Hypoparathyroidism: 26-Week Results From the Phase 3 PaTHway Trial. J Bone Miner Res. 2023;38(1):14-25. doi:10.1002/jbmr.4726
4. Clarke BL, Khan AA, Rubin MR, et al. Efficacy and Safety of TransCon PTH in Adults with Hypoparathyroidism: 52-Week Results From the Phase 3 PaTHway Trial. J Clin Endocrinol Metab. Published online October 8, 2024. doi:10.1210/clinem/dgae693

Related Policies

Currently there are no related policies.

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created	02/2025