Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCEND086.0425	**ENDOCRINE AND METABOLIC DRUGS** **YORVIPATH®** (palopegteriparatide injection)
Effective Date: 6/1/2025	**Review/Revised Date**: 02/25 (MTW)
Original Effective Date: 02/25	**P&T Committee Meeting Date**: 12/24, 04/25
Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:
Providence Health Plan and Providence Health Assurance as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:
Commercial
Medicaid

POLICY CRITERIA:

COVERED USES:
All Food and Drug Administration (FDA)-Approved Indications

REQUIRED MEDICAL INFORMATION:
For initiation of therapy all the following criteria must be met:
1. Confirmed diagnosis of chronic hypoparathyroidism of postsurgical, autoimmune, genetic, or idiopathic origins, for at least 26 weeks, based on hypocalcemia in the setting of inappropriately low serum parathyroid hormone levels. Note: Coverage will not be provided in the case of acute postsurgical hypoparathyroidism
2. Documentation that patient is currently receiving conventional therapy, including active vitamin D (calcitriol) and elemental calcium
3. Provider attestation that patient's disease cannot be adequately controlled on conventional therapy alone or that conventional therapy causing significant side effects

For patients established on therapy all the following criteria must be met (Note: Medications obtained as samples, coupons, or any other method of obtaining medications outside of an established health plan benefit are NOT considered established on therapy):
1. Documentation of a recent (within the last three months) albumin-corrected serum calcium in the lower-half of the normal reference range or just below the normal reference range
2. One of the following:

a. Patient no longer requires active vitamin D or therapeutic doses of calcium, OR
b. Patient has had a significant reduction in required dosages of active vitamin D or therapeutic doses of calcium and is still actively titrating doses of palopegteriparatide (Yorvipath®)

EXCLUSION CRITERIA:
Use of osteoporosis therapies known to influence calcium and bone metabolism less than two years before screening (such as abaloparatide or teriparatide).

AGE RESTRICTIONS:
May be approved for patients aged 18 years and older.

PRESCRIBER RESTRICTIONS:
Must be prescribed by, or in consultation with, an endocrinologist.

COVERAGE DURATION:
Initial authorization and reauthorization will be approved for one year.

QUANTITY LIMIT:
Two pens per 28 days

Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION: Palopegteriparatide releases PTH(1-34) which exerts effects on the parathyroid hormone 1 receptor (PTH1R). This receptor is highly expressed on osteoblasts, osteocytes, renal tubular cells, and several other tissues. Similar to endogenous PTH, PTH(1-34) helps maintain extracellular calcium and phosphate homeostasis by increasing serum calcium and decreasing serum phosphate. These

effects are mediated by stimulating bone turnover to mobilize calcium and phosphate from bone, promoting renal calcium reabsorption and phosphate excretion, and facilitating active vitamin D synthesis, in turn increasing intestinal absorption of calcium and phosphate.

FDA APPROVED INDICATIONS:
Treatment of hypoparathyroidism in adults. Limitations of Use:

- Not studied for acute post-surgical hypoparathyroidism
- Titration scheme only evaluated in adults who first achieved an albumin-corrected serum calcium of at least 7.8 mg/dL using calcium and active vitamin D treatment

POSITION STATEMENT:

- Hypoparathyroidism (HP) is a rare disorder causing insufficient levels of parathyroid hormone, which leads to low calcium and elevated phosphate levels in the blood. Symptoms of HP depend on the severity of disease and can cause potentially life-threatening complications such as arrhythmias and laryngospasms. Other symptoms of chronic HP can include cataracts, increased bone mineral density, basal ganglia calcifications that cause movement disorders, dental abnormalities, and dermatologic manifestations (such as dry skin, brittle hair and nails). By correcting hypocalcemia, many of these symptoms can be resolved.
- HP can be caused by postsurgical, autoimmune, and genetic disorders. Damage to the parathyroid gland does not always result in chronic HP and is often acute, lasting for days to months. Guidelines typically consider HP to be chronic after 6 to 12 months. Laboratory testing confirms diagnosis with the presence of hypocalcemia, low PTH, hyperphosphatemia, and normal magnesium. Albumin levels must also be drawn to ensure corrected calcium levels are used if there is an abnormality in albumin levels.
- The goal of treating HP is to achieve normal serum calcium concentration, ideally in the low end of normal. Conventional treatment typically consists of oral calcium (most commonly calcium carbonate and calcium citrate) and vitamin D supplementation (most commonly calcitriol). It can be difficult to achieve and maintain serum calcium levels with calcium and vitamin D supplementation and this can be further complicated by side effects, including hypercalciuria, nephrocalcinosis, renal failure, and soft-tissue calcification. The only other parathyroid analogue approved for hypoparathyroidism is Natpara® (recombinant human PTH [1-84]) which was recalled in 2019 and being discontinued.

<u>Clinical Trial</u>

- Palopegteriparatide was approved based on results from the randomized, double-blind, placebo controlled, parallel group Phase 3 PaTHway trial conducted over 26 weeks.
    - Inclusion criteria: age > 18 years, postsurgical, autoimmune, genetic, or idiopathic chronic HP for >26 weeks, based on hypocalcemia in the setting of inappropriately low serum PTH levels, treated with calcitriol ≥0.5 µg/d or alfacalcidol ≥1.0 µg/d in addition to elemental calcium ≥800 mg/d for ≥12 weeks before screening, and on stable doses for ≥5 weeks, must achieve an albumin-adjusted serum calcium of ≥7.8 mg/dL, 25 (OH) vitamin D level of 20-80 ng/mL, and a magnesium level of ≥1.3 mg/dL prior to randomization
    - Exclusion criteria: use of osteoporosis therapies known to influence calcium and bone metabolism, i.e., bisphosphonate, denosumab, raloxifene, or romosozumab therapies within two years prior to screening.
- 82 patients randomized 3:1 to receive conventional therapy (calcium and active vitamin D) along with palopegteriparatide PTH (n=61) at a starting dose of 18 mcg/day or placebo (n=21).
- Primary efficacy endpoint: proportion of subjects with albumin-adjusted serum calcium within the normal range, independence from active vitamin D and independence from therapeutic doses of calcium (i.e., taking calcium supplements < 600 mg/day), no increase in prescribed study drug within 4 weeks prior to Week 26 visit.
    - After 26 weeks of blinded treatment, 79% of participants receiving palopegteriparatide PTH (95% CI 66,88) vs. 5% receiving placebo (95% CI 0.1,24) meet the primary composite endpoint ($p < 0.0001$).
    - Breakdown of participants meeting each component of composite endpoint: 80.3% of patients in the palopegteriparatide PTH group had albumin-adjusted serum calcium within normal range vs. 47.6% in the placebo group; 98.4% had independence from active vitamin D in the palopegteriparatide PTH group vs. 23.8% in the placebo group; 93.5% had independence from therapeutic doses of calcium vs. 5% in the placebo group; and 93.5 % had no increase in the prescribed study drug in the final four weeks of the period.
    - A greater of proportion of participants treated with palopegteriparatide PTH (60.7%) than placebo (28.6%) achieved normal 24-hour urine calcium excretion.
- In a post hoc analysis of renal function, it was determined that palopegteriparatide treatment was associated with significantly improved eGFR at week 52. Further investigation of palopegteriparatide for the preservation renal function in hypo-PTH is needed.

REFERENCE/RESOURCES:

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2. Yorvipath® In: DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Reuters (Healthcare) Inc. Updated periodically. Accessed October 29, 2024
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7. Rejnmark L, Gosmanova EO, Khan AA, et al. Palopegteriparatide Treatment Improves Renal Function in Adults with Chronic Hypoparathyroidism: 1-Year Results from the Phase 3 PaTHway Trial. Adv Ther. 2024 Jun;41(6):2500-2518. doi: 10.1007/s12325-024-02843-8. Epub 2024 Apr 30. PMID: 8691316; PMCID: PMC11133178