Original Effective Date: 03/28/2025
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Last P&T Approval/Version: 01/29/2025
Next Review Due By: 01/2026
Policy Number: C29043-A

Yorvipath (palopegteriparatide)

PRODUCTS AFFECTED

Yorvipath (palopegteriparatide)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Hypoparathyroidism

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. HYPOPARATHYROIDISM:
   1. Documentation of diagnosis of hypoparathyroidism
      AND

2. Documentation that member's 25-hydroxyvitamin D stores are sufficient (levels of >20 nmol/L to < 80 nmol/L are considered adequate in healthy individuals)
   AND
3. Documentation that member's albumin-corrected serum calcium is above 7.8 mg/dL
   AND
4. Prescriber attests that Yorvipath is not being used for acute hypoparathyroidism post-surgery.
   AND
5. Documentation of trial and failure of maximally tolerated calcium supplements and active or analog forms of vitamin D (e.g., calcitriol, ergocalciferol, cholecalciferol) alone. Documentation of medication(s) tried and maximally tolerated dosing is required.
   AND
6. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Yorvipath (palopegteriparatide) include: hypersensitivity to any component of the product]
   AND
7. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal

CONTINUATION OF THERAPY:

A. HYPOPARATHYROIDISM:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Documentation the member can maintain serum calcium within the normal range without the use of active Vitamin D analogs (calcitriol)
   AND
3. Documentation member has an albumin-corrected total serum calcium concentration between 7.8 mg/dL and 10.6 mg/dL
   AND
4. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a board-certified endocrinologist [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

18 years of age and older

QUANTITY:

Starting dose: 18 mcg once daily
Maximum daily dose: 30 mcg once daily
See Appendix for titration details

PLACE OF ADMINISTRATION:

The recommendation is that injectable medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Subcutaneous

DRUG CLASS:
Hypoparathyroid Treatment - Parathyroid Hormone Analogs

FDA-APPROVED USES:
Yorvipath is indicated for the treatment of hypoparathyroidism in adults.
Limitations of Use: Yorvipath was not studied for acute post-surgical hypoparathyroidism. Yorvipath's titration scheme was 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.

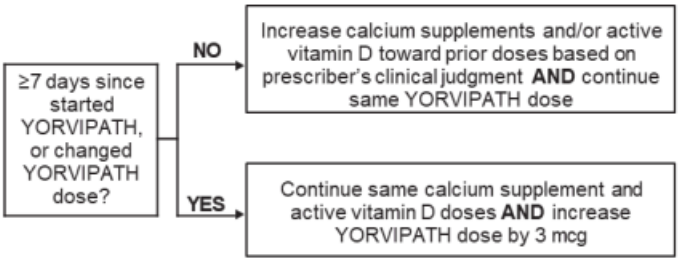
COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

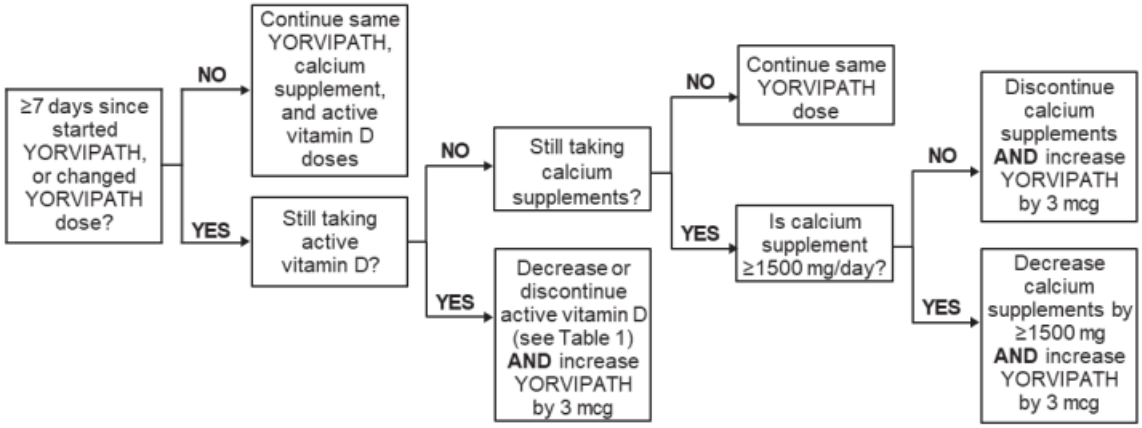
APPENDIX:
The starting dose of Yorvipath is 18 mcg injected once daily in the abdomen or front of the thigh. When starting Yorvipath, decrease dose of active vitamin D (calcitriol) by 50% if serum calcium is between 7.8 to 8.3 mg/dL. If serum calcium is above or equal to 8.3 mg/dL and current calcitriol dose is greater than 1 mcg/day, decrease the dose of active Vitamin D (calcitriol) by 50% (may discontinue calcitriol if current dose is less than or equal to 1 mcg/day). The dose may be increased by 3 mcg every 7 days up to a maximum daily dose of 30 mcg daily. The dose may also be decreased by 3 mcg every 3 days. The recommended dose range is 6 to 30 mcg once daily. Refer to Figure 1 for the titration scheme provided by the manufacturer (Yorvipath, 2024).

Figure 1: Titration of YORVIPATH, Active Vitamin D, and Calcium Supplements

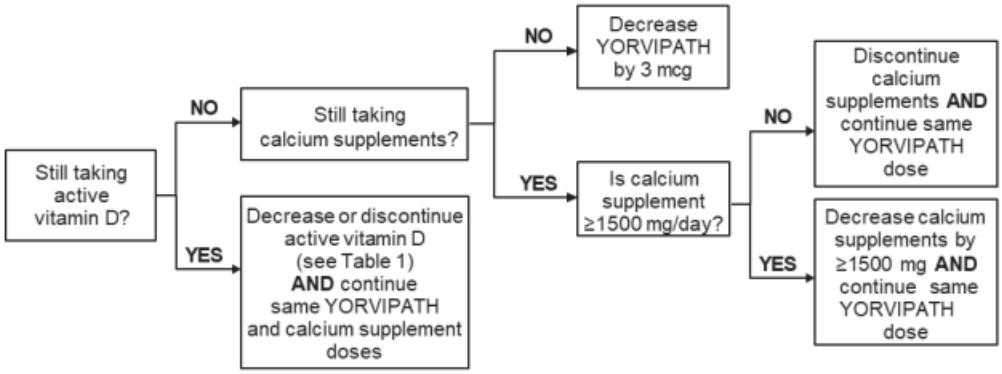
Albumin-Corrected Serum Calcium <8.3 mg/dL:



Albumin-Corrected Serum Calcium 8.3 to 10.6 mg/dL:



Albumin-Corrected Serum Calcium 10.7 to 11.9 mg/dL:



BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Yorvipath (palopegteriparatide) is a parathyroid hormone analog injection, intended to regulate internal calcium levels. It is used in patients who fail to maintain calcium levels in the normal range of 7.8 to 10.6 mg/dL via calcium supplementation and active or inactive Vitamin D supplementation. It works by regulating serum calcium and phosphate levels via promoting bone turnover, increasing renal calcium reabsorption while decreasing phosphate reabsorption, and increasing calcium absorption in the intestines. Hypoparathyroidism is a condition caused by loss of function of the parathyroid gland and reduced secretion of parathyroid hormone. This is commonly caused by a parathyroidectomy, various autoimmune conditions, trauma or congenital disease.

Hypoparathyroidism is a rare condition with an estimated incidence of 37 new cases per 100,000 people per year in the US. Subsequently, this condition has been designated by the FDA as an orphan disease. This condition is characterized by low or normal levels of endogenous parathyroid hormone (PTH) and the presence of hypocalcemia. PTH is released from the parathyroid glands in response to low levels of serum calcium. This results in promotion of bone turnover, increased renal calcium reabsorption with decreased phosphate reabsorption, and increased calcium absorption in the intestines with a goal of returning serum calcium to normal levels. Patients with hypoparathyroidism lack the ability to regulate their calcium levels resulting in symptoms of hypocalcemia which may include acute symptoms (paresthesia, seizures, cardiac arrhythmias and laryngeal spasms) and chronic symptoms (cardiomyopathy, extracellular calcification, increased bone density, increased fracture risk, increased risk of kidney stones, and renal impairment).

Current therapy of hypoparathyroidism is characterized by initial management with oral calcium and active or inactive Vitamin D supplementation. The goal of this treatment is to correct hypocalcemia, prevent hypercalcemia, and prevent complications or symptoms from occurring. This treatment option is not effective for all patients as the dosing is often difficult to adjust based on serum calcium and may be difficult to tolerate. This option also does not address the underlying pathophysiology of hypoparathyroidism and its effects on bone turnover and renal regulation of calcium levels. Previously, a parathyroid analog, Natpara, was FDA-approved in 2015 to meet this need. Issues with manufacturing resulted in the eventual discontinuation of this medication with an expected withdrawal from the market at the end of 2024.

The effectiveness of Yorvipath was studied in a phase 3, randomized, double-blind, placebo-controlled, 26-week trial with 82 participants (PaTHway trial). Participants were randomized to either receive placebo (n=21) or Yorvipath (n=62) with a starting dose of 18 mcg/day. Prior to the trial start, participants underwent a 4-week screening period where calcium and Vitamin D supplement dosing was manipulated with a goal of patients having a calcium level between 7.8 and 10.6 mg/dL, a 25(OH) vitamin D level between 20 to 80 ng/mL and a magnesium level ≥1.3 mg/dL and below the upper limit of normal. Participants initially received both active Vitamin D and calcium supplementation along with Yorvipath, both of which were titrated according to albumin-adjusted calcium levels as mentioned previously.

At baseline, the majority of participants were Caucasian (89%), female (78%), with a mean age of 49. Most hypoparathyroidism diagnoses in the study were a result of neck surgery (85%), though there were participants with various other etiologies. For the Yorvipath group the mean baseline serum calcium was 8.8 mg/dL compared to 8.6 mg/dL for the placebo group. The mean baseline dose of elemental calcium was 1839 mg/day among the participants. Mean baseline dosing of calcitriol was 0.75 mcg/day (n=70) and, for patients receiving alfacalcidol (n=12), 2.3 mcg/day.

Effectiveness was analyzed based on the fraction of participants who achieved all the following after 26 weeks: Serum calcium in the normal range of 8.3 to 10.6 mg/dL, required no active Vitamin D therapy and less than 600 mg/day of calcium since week 22, no subsequent increase in Yorvipath dosing after week 22, no missing active Vitamin D or calcium data since week 22 and a Yorvipath dose of 30 mcg/day or less during the study period. At week 26 investigators found that 42 of 61 patients in the Yorvipath group met the efficacy criteria compared with 1 of 21 patients in the placebo group. They found a statistically significant treatment difference of 64.2% (95% CI: 49.5%, 78.8%).

Adverse effects that occurred during the study period were also reported. Adverse reactions that occurred in over 5% of patients include: injection site reactions, orthostatic hypotension with associated symptoms, back pain, headache, diarrhea, oropharyngeal pain, and hypercalcemia. Symptomatic hypercalcemia occurred in 8% of patients within the first 3 months.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Yorvipath are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Yorvipath include: hypersensitivity to any component of the product.

OTHER SPECIAL CONSIDERATIONS:
Do not use more than one injection to achieve the desired dose. Using more than one injection increases the risk of either hypercalcemia or hypocalcemia.

If a dose is missed by more than 12 hours, the dose may be skipped and resumed as scheduled the next day. If under 12 hours, take the dose as soon as possible.

If Yorvipath is prescribed to patients taking Digoxin, monitor for signs and symptoms of Digoxin toxicity and measure Digoxin levels regularly.

Patient who had taken any medication that effects calcium stores in the past two years, such as various osteoporosis medications, were excluded from the study. Closely monitor patients taking any medication that may effect serum calcium.

Patients at an increased risk for osteosarcoma (which includes those with Paget's disease of bone or unexplained elevations of alkaline phosphatase, pediatric and young adult patients with open epiphyses, patient with a history of skeletal malignancies, patients with hereditary disorders predisposing to osteosarcoma or patients with a history of prior external beam or implant radiation therapy involving the skeleton) should be cautious when using Yorvipath due to an increased risk of osteosarcoma observed in animal studies that included parathyroid hormone analogs.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Yorvipath SOPN 168MCG/0.56ML
Yorvipath SOPN 294MCG/0.98ML
Yorvipath SOPN 420MCG/1.4ML

REFERENCES

1. Yorvipath (palopegteriparatide) injection [prescribing information]. Copenhagen, Denmark: Ascendis Pharma; August 2024.
2. Bilezikian J. P. (2020). Hypoparathyroidism. The Journal of clinical endocrinology and metabolism, 105(6), 1722–1736. https://doi.org/10.1210/clinem/dgaa113
3. Brandi, Maria Luisa, et al. Management of Hypoparathyroidism: Summary Statement and Guidelines. J Clin Endocrinol Metab. June 2016. 101(6):2273-2283.
4. Clarke, B. L., Brown, E. M., et al. (2016). Epidemiology and Diagnosis of Hypoparathyroidism. The Journal of clinical endocrinology and metabolism, 101(6), 2284–2299. https://doi.org/10.1210/jc.2015-3908
5. Sell, J., Ramirez, S., & Partin, M. (2022). Parathyroid Disorders. American family physician, 105(3), 289–298.

SUMMARY OF REVIEW/REVISIONS	DATE
NEW CRITERIA CREATION	Q1 2025