palopegteriparatide (Yorvipath®)

Policy # 00921
Original Effective Date: 04/01/2025
Current Effective Date: 04/01/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider palopegteriparatide (Yorvipath®)‡ for the treatment of hypoparathyroidism to be **eligible for coverage.****

Patient Selection Criteria
Coverage eligibility for palopegteriparatide (Yorvipath) will be considered when the following criteria are met:

Initial Authorization:

- Patient has a diagnosis of chronic hypoparathyroidism as evidenced by documentation of hypocalcemia and parathyroid hormone (PTH) concentrations below the lower limit of the normal reference range for at least 6 months; AND
- Patient is 18 years of age or older; AND
- Patient has tried and had an inadequate response to maximally tolerated oral calcium AND vitamin D supplements unless there is clinical evidence or patient history that suggests the use of oral calcium AND vitamin D supplements will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has sufficient 25-hydroxyvitamin D stores (at baseline before initiating Yorvipath therapy) according to the prescriber; AND
- Patient has an albumin-adjusted serum calcium ≥ 7.8 mg/dL (at baseline before initiating Yorvipath therapy) according to the prescriber; AND
- Patient does NOT have acute post-surgical hypoparathyroidism

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross Blue Shield Association. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.

© 2025 Louisiana Blue

palopegteriparatide (Yorvipath®)

Policy # 00921
Original Effective Date: 04/01/2025
Current Effective Date: 04/01/2025

Continuation

- Patient has received an initial authorization for the requested medication; AND
- Patient has experienced a positive clinical response to treatment (including, but not limited to, a reduction in the patient's oral calcium dose, reduction in the patient's active vitamin D dose and/or maintenance of a stable albumin-corrected total serum calcium concentration.) *(Note: This specific patient selection criterion is an additional company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

When Services Are Considered Not Medically Necessary

Based on the review of available data, the Company considers the use of palopegteriparatide (Yorvipath) when the patient has not tried and had an inadequate response to maximally tolerated oral calcium AND vitamin D supplements to be **not medically necessary.****

Based on review of available data, the Company considers the continued use of palopegteriparatide (Yorvipath) when the patient has not experienced a positive clinical response to treatment to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of palopegteriparatide (Yorvipath) when the patient selection criteria are not met (except those noted to be **not medically necessary****) to be **investigational.***

Background/Overview

Yorvipath is a parathyroid hormone analog (PTH [1-34]) indicated for the treatment of hypoparathyroidism in adults. Yorvipath is available in a prefilled, disposable, 14-dose pen-injector. Each pack contains two prefilled pens and 28 needles for 28 injections. The recommended dosage range is 6 to 30 mcg administered as a subcutaneous injection once daily. Yorvipath's maintenance dosage is individualized based on serum calcium levels. The recommended starting dosage is 18 mcg once daily and is titrated in 3 mcg increments or decrements with the goal of maintaining serum calcium within the normal range without the need for active vitamin D (e.g., calcitriol) or therapeutic calcium doses (elemental calcium > 600 mg/day). Calcium supplementation sufficient to meet daily dietary requirements may be continued. Once the Yorvipath maintenance dosage is achieved, serum calcium levels should be measured at a minimum of every 4 to 6 weeks or as indicated for symptoms of hypocalcemia or hypercalcemia. Laboratory testing confirming serum 25(OH) vitamin D is within the normal range and albumin-corrected serum calcium is ≥ 7.8 mg/dL should be conducted within two weeks prior to initiating treatment with Yorvipath. The approved dosing titration scheme for

palopegteriparatide (Yorvipath®)

Policy # 00921
Original Effective Date: 04/01/2025
Current Effective Date: 04/01/2025

Yorvipath has only been evaluated in adults who first achieved an albumin-corrected serum calcium of at least 7.8 mg/dL utilizing calcium and active vitamin D treatment. Yorvipath has not been studied for acute post-surgical hypoparathyroidism.

Hypoparathyroidism
Parathyroid hormone is one of the major hormones that is involved in the regulation of serum calcium. It exerts its effects via the bone, kidney, and gastrointestinal tract. Hypoparathyroidism develops when there is destruction of the parathyroid glands, abnormal gland development, altered regulation of parathyroid hormone production, or impaired parathyroid hormone action. When parathyroid levels are low, hypocalcemia develops. Renal, skeletal, cardiovascular, neuromuscular, and neurological/neuropsychiatric complications are commonly observed in patients with chronic hypoparathyroidism. Cataracts, dental abnormalities, and dermatologic manifestations can also occur. Guidelines currently recommend conventional therapy with oral calcium supplementation and active vitamin D as first-line therapy. PTH replacement is recommended in patients who are not able to be adequately managed with conventional therapy (calcium and active vitamin D).

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Yorvipath is approved for the treatment of hypoparathyroidism in adults.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

The effectiveness and safety of Yorvipath in adults with chronic hypoparathyroidism were evaluated in a 26-week, randomized, double-blind, placebo-controlled, phase 3 study which was conducted in 82 patients with hypoparathyroidism. Prior to randomization, all patients underwent an approximate 4-week screening period in which calcium and active vitamin D supplements were adjusted to achieve an albumin-corrected serum calcium concentration between 7.8 and 10.6 mg/dL, a magnesium concentration ≥ 1.3 mg/dL and below the upper limit of the reference range, and a 25(OH) vitamin D concentration between 20 to 80 ng/mL. Patients were randomized (3:1) to receive either Yorvipath (n = 61) or placebo (n = 21), at a starting dose of 18 mcg/day, co-administered with conventional therapy (calcium and active vitamin D). Yorvipath and conventional therapy were subsequently titrated according to the albumin-corrected serum calcium levels. Efficacy was assessed based on the proportion of subjects who achieved all of the following at Week 26: an albumin-corrected serum calcium level in the normal range (8.3 to 10.6 mg/dL); independence from conventional therapy (defined as requiring no active vitamin D and ≤ 600 mg/day of calcium

supplementation [including no "as needed" doses] since Week 22); no increase in the study drug dose since Week 22; no missing active vitamin D and calcium data since Week 22; and study drug dose of ≤ 30 mcg QD during the 26-week treatment period. At Week 26, 68.9% of patients met the efficacy endpoint compared with 4.8% of patients given placebo.

References

1. Yorvipath [package insert]. Ascendis Pharma, Endocrinology, Inc. Princeton, New Jersey. Updated 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.
3. Yorvipath Drug Evaluation. Express Scripts. Updated August 21, 2024.

Policy History

Original Effective Date: 04/01/2025
Current Effective Date: 04/01/2025
03/06/2025 Medical Policy Committee review
03/12/2025 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 03/2026

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

palopegteriparatide (Yorvipath®)

Policy # 00921
Original Effective Date: 04/01/2025
Current Effective Date: 04/01/2025

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.