parathyroid hormone (Natpara®)

Policy # 00629
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Current Effective Date: 09/13/2021

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 parathyroid hormone (Natpara®)‡ as an adjunct therapy for the control of hypocalcemia in patients with hypoparathyroidism to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for parathyroid hormone (Natpara) will be considered when the following criteria are met:

Initial:

- Patient has a diagnosis of hypoparathyroidism; AND
- The patient cannot be well-controlled on calcium supplements and active forms of vitamin D alone; AND
- Patient's 25-hydroxyvitamin D stores are sufficient [before initiating parathyroid hormone (Natpara) therapy] per the prescribing physician; AND
- Patient's serum calcium concentration is > 7.5 mg/dL before initiating parathyroid hormone (Natpara) therapy; AND
- Patient does NOT have acute post-surgical hypoparathyroidism; AND
- Patient does NOT have hypoparathyroidism caused by calcium sensing receptor mutations.

Continuation:

- Patient has met initial coverage criteria; AND
- Patient's 25-hydroxyvitamin D stores are sufficient [during parathyroid hormone (Natpara) therapy] per the prescribing physician; AND

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- Patient is responding to parathyroid hormone (Natpara) therapy (e.g., reduction in the patient's oral calcium dose; reduction in the patient's active vitamin D dose; maintenance of a stable albumin-corrected total serum calcium concentration), as determined by the prescriber.
  *(Note: This specific patient 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 review of available data, the Company considers the use of parathyroid hormone (Natpara) when the patient is NOT responding to parathyroid hormone (Natpara) therapy 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 parathyroid hormone (Natpara) when the patient selection criteria are not met to be **investigational*** (with the exception of the criterion denoted above as **not medically necessary****).

Background/Overview

Natpara is a parathyroid hormone approved as an adjunct to calcium and vitamin D therapy to control hypocalcemia in patients with hypoparathyroidism. Natpara is recommended only for patients who cannot be well-controlled on calcium supplements and active forms of vitamin D alone due to the potential risk of osteosarcoma. Natpara was not studied in patients with hypoparathyroidism caused by calcium receptor mutations, nor was it studied in patients with acute post-surgical hypoparathyroidism. The dose of Natpara should be individualized to achieve a serum calcium level in the lower half of the normal range. Prior to starting Natpara, the prescriber should confirm that the patient's vitamin D stores are sufficient and that serum calcium is above 7.5 mg/dL. The starting dose of Natpara is 50 mcg given once daily. When starting therapy, the active vitamin D dose should be decreased by 50% if the serum calcium is above 7.5 mg/dL. Monitor serum calcium levels every 3 to 7 days after starting or adjusting the Natpara dose and when adjusting either active vitamin D

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or calcium supplement doses while using Natpara. Natpara is supplied in four strengths: 25 mcg, 50 mcg, 75 mcg, or 100 mcg.

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 is brought upon 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. Hypocalcemia can result in seizures, heart failure, laryngospasm, or a host of other issues. The initial management of patients with chronic hypoparathyroidism includes the use of calcium and vitamin D supplementation. The addition of Natpara is indicated in those whose hypocalcemia cannot be controlled with calcium and vitamin D supplementation alone.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Natpara was approved in early 2015 as an adjunct to calcium and vitamin D therapy to control hypocalcemia in patients with hypoparathyroidism.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Natpara was evaluated in a 24-week, randomized, double-blind, placebo-controlled, multicenter trial. In this trial, patients with established hypoparathyroidism receiving calcium and active forms of vitamin D were randomized to Natpara (n=84) or placebo (n=40). Patients with hypoparathyroidism due to calcium-sensing receptor mutations were excluded from the trial. Before randomization, participants entered a 2-16 weeks run-in phase. In this phase, calcium supplement and active vitamin D doses were adjusted to target an albumin-corrected serum calcium

concentration between 8.0 and 9.0 mg/dL and 25-hydroxyvitamin D was replaced in patients with insufficient stores. At randomization, active forms of vitamin D were reduced by 50% and patients were randomized to Natpara 50 mcg daily or placebo. Randomization was followed by a 12-week Natpara titration phase and a 12-week Natpara dose maintenance phase. During the titration phase Natpara was increased by 25 mcg increments every four weeks up to a maximum of 100 mcg. At the end of treatment, 56% of subjects randomized to Natpara were receiving 100 mcg of Natpara per day, 26% were receiving 75 mcg of Natpara per day, and 18% were receiving 50 mcg of Natpara per day. A responder was defined as an individual who had: at least a 50% reduction from baseline in the dose of active vitamin D, at least a 50% reduction from baseline in the dose of oral calcium supplementation and an albumin-corrected total serum calcium concentration between 7.5 mg/dL and 10.6 mg/dL. At the end of treatment, significantly more subjects treated with Natpara (54.8%) compared to placebo (2.5%) met the response criterion ($p<0.001$).

References

1. Natpara [package insert]. Shire-NPS Pharmaceuticals. Lexington, MA. Updated July 2016.
2. Hypoparathyroidism. UpToDate. Accessed 7/18/2018.
3. Natpara. Express Scripts Prior Authorization Document. Updated April 2018.

Policy History

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08/09/2018	Medical Policy Committee review
08/15/2018	Medical Policy Implementation Committee approval. New policy.
08/01/2019	Medical Policy Committee review
08/14/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/06/2020	Medical Policy Committee review
08/12/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/05/2021	Medical Policy Committee review

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08/11/2021 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Next Scheduled Review Date: 08/2022

*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 the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated 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.

**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.

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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.

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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.