VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Natpara Prior Authorization Policy
- Natpara® (parathyroid hormone for subcutaneous injection – Shire-NPS Pharmaceuticals)

REVIEW DATE: 04/21/2021

OVERVIEW

Natpara, a replica of the endogenous parathyroid hormone, is indicated as an **adjunct to calcium and vitamin D to control hypocalcemia in patients with hypoparathyroidism**.[1] There are several limitations to Natpara use: because of the potential risk of osteosarcoma, Natpara is recommended only for patients who cannot be well-controlled on calcium supplements and active forms of vitamin D alone; it was not studied in patients with hypoparathyroidism caused by calcium-sensing receptor mutations; and it was not studied in patients with acute post-surgical hypoparathyroidism. The dose of Natpara should be individualized based on total serum calcium (albumin-corrected) and 24-hour urinary calcium excretion. The recommended dose is the minimum dose required to prevent both hypocalcemia and hypercalciuria. And, this dose will generally be the dose that maintains total serum calcium (albumin-corrected) within the lower half of the normal range (i.e., between 8 and 9 mg/dL) without the need for active forms of vitamin D and calcium supplementation sufficient and individualized to meet the patient's daily requirements.

Before initiating and during therapy with Natpara, 25-hydroxyvitamin D stores should be sufficient.[1] In addition, before initiating Natpara, serum calcium concentration should be > 7.5 mg/dL In the pivotal study, a responder to Natpara therapy was defined as an individual who had: ≥ 50% reduction from baseline in the dose of active vitamin D, ≥ 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.[1]

Natpara has a Boxed Warning about the risk of osteosarcoma.[1] Parathyroid hormone has been shown to increase the incidence of osteosarcoma in male and female rats; the risk was dependent on dose and treatment duration. A risk to humans could not be excluded. Natpara is available only through a restricted Risk Evaluation and Mitigation Strategy (REMS) program; only certified healthcare providers can prescribe and only certified pharmacies can dispense Natpara.

Note: Natpara continues to be unavailable except to select patients through a Special Use Program. On March 31, 2021, the manufacturer (Takeda) said Natpara is not expected to be available before March 31, 2022.[13]

Disease Overview

Hypoparathyroidism is a rare endocrine disorder that affects approximately 60,000 individuals in the US.[2,3] This condition is characterized by low calcium and high phosphate levels and low or inappropriately normal parathyroid hormone level.[4] The parathyroid hormone plays a critical role in maintaining calcium homeostasis and bone metabolism (osteoclasts and osteoblasts).[3,5-7] In some cases, the parathyroid glands produce insufficient parathyroid hormone and in other cases, the parathyroid glands have been removed.[2,5,8] The goals of treatment of hypoparathyroidism are to maintain serum calcium and the calcium-phosphate product within the normal range and avoid hypercalciuria.[4] The standard of care includes oral calcium and (active or parental) vitamin D to manage the hypocalcemia that results from the condition.[6-8] While these products maintain serum calcium concentration within normal limits and minimize the symptoms of hypocalcemia, they do not address the physiologic aspects of hypoparathyroidism. Additionally, there are

long-term complications associated with calcium and vitamin D therapy, including renal function deterioration, renal stones, and soft tissue calcification.[3,6,9-11]

Guidelines/Recommendations

A consensus statement released in 2019 notes the use of calcium supplements and active vitamin D as the conventional therapy for hypoparathyroidism.[12] Although these therapies address the hypocalcemic aspect of hypoparathyroidism, they fail to provide a physiologic replacement of parathyroid hormone. Natpara therapy should be considered in patients experiencing inadequate control of serum calcium; patients who require > 2.5 g of calcium or > 1.5 µg of calcitriol per day to control serum calcium or symptoms; patients with hypercalciuria, renal stones, nephrocalcinosis, stone risk or reduced creatinine clearance or estimated glomerular filtration rate (eGFR) (< 60 mL/min); or patients with hyperphosphatemia and/or calcium-phosphate product > 55 mg^2/dL^2 or 4.4 $mmol^2/L^2$. Natpara therapy may also be beneficial in patients who have malabsorption or who are intolerant of large doses of oral calcium supplements or who are noncompliant with taking several tablets a day.

The First International Conference on the Management of Hypoparathyroidism provided some guidelines on the management of this condition (2016).[9] Conventional management of chronic hypoparathyroidism includes use of calcium supplements, active vitamin D or analogs, magnesium, thiazide diuretics (when necessary to help manage hypercalciuria and low salt diet), and phosphate binders and low phosphate diet (if necessary to control hyperphosphatemia). Natpara therapy may be considered in patients with well-established chronic hypoparathyroidism of any etiology except for autosomal dominant hypocalcemia; variable and inconsistent control of the serum calcium with frequent episodes of hypo- and hypercalcemia; nephrolithiasis, nephrocalcinosis, or reduced creatinine clearance or eGFR to < 60 mL/min; hypercalciuria and/or other biochemical indices or renal stone risk; persistently elevated serum phosphate and/or calcium-phosphate product (> 55 mg^2/dL^2 or 4.4 $mmol^2/L^2$); excessive amounts of oral medications required to control symptoms such as > 2.5 g of calcium or > 1.5 µg of active vitamin D, or both; and a gastrointestinal tract disorder that might lead to variable calcium and vitamin D absorption.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Natpara. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Natpara as well as the monitoring required for adverse events and long-term efficacy, approval requires Natpara to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Natpara is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Chronic Hypoparathyroidism.** Approve for 3 years if the patient meets ONE of the following conditions (A or B):
   - **A)** Initial Therapy. Approve if the patient meets ALL of the following criteria (i, ii, iii, and iv):
     - **i.** Patient cannot be well-controlled on calcium supplements and active forms of vitamin D alone; AND
     - **ii.** Patient's 25-hydroxyvitamin D stores are sufficient (before initiating Natpara therapy) according to the prescriber; AND
     - **iii.** Patient's serum calcium concentration is > 7.5 mg/dL before initiating Natpara therapy; AND
     - **iv.** The medication is prescribed by or in consultation with an endocrinologist.
   - **B)** Patient is Currently Receiving Natpara. Approve if the patient meets ALL of the following criteria (i, ii, and iii):
     - **i.** Patient cannot be well-controlled on calcium supplements and active forms of vitamin D alone; AND
     - **ii.** Patient's 25-hydroxyvitamin D stores are sufficient (during Natpara therapy) according to the prescriber; AND
     - **iii.** Patient is responding to 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), according to the prescriber.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Natpara is not recommended in the following situations:

1. **Acute Post-Surgical Hypoparathyroidism.** Natpara was only studied in patients with chronic hypoparathyroidism.

2. **Hypoparathyroidism Caused by Calcium-Sensing Receptor Mutations.** Natpara was not studied in this patient population.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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