PRIOR AUTHORIZATION POLICY

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

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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: due to 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.

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.

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 for select patients through a Special Use Program. On March 22, 2022, the manufacturer (Takeda) released a statement indicating that Natpara's return to the commercial market is indefinitely delayed.[2]

Guidelines/Recommendations

A consensus statement released in 2019 notes the use of calcium supplements and active vitamin D as the conventional therapy for hypoparathyroidism.[3] Natpara therapy should be considered in patients experiencing inadequate control of serum calcium; patients who require > 2.5 g of calcium or > 1.5 mcg 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).[4] 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, initial 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 Indication

1. **Chronic Hypoparathyroidism.** Approve for 1 year 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.

REFERENCES

1. Natpara® subcutaneous injection [prescribing information]. Lexington MA: Shire-NPS/Takeda; July 2020.
2. Takeda provides Natpara regulatory update. Available at: https://www.takeda.com/495347/siteassets/en-us/home/newsroom/natpara/2022-03-22-natpara-update-us-crl-statement.pdf. Accessed on April 15, 2022.
3. Khan AA, Koch CA, Uum SV, et al. Standards of care for hypoparathyroidism in adults: a Canadian and international consensus. *Eur J Endocrinol*. 2019;180:P1-P23.
4. Brandi ML, Bilezikian JP, Shoback D, et al. Management of hypoparathyroidism: summary statement and guidelines. *J Clin Endocrinol Metab*. 2016;101:2273-2283.