

PRIOR AUTHORIZATION POLICY

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

DATE REVIEWED: 04/17/2019

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 and 24-hour urinary calcium excretion. The initial dose of Natpara is 50 mcg once daily (QD) given as a subcutaneous injection; the dose may be decreased to as low as 25 mcg/day or increased to the maximum daily dose of 100 mcg.

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

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

Guidelines/Recommendations

The First International Conference on the Management of Hypoparathyroidism provided some guidelines on the management of this condition (2016).⁹ The goals of chronic management therapy are: prevent signs and symptoms of hypocalcemia; maintain the serum calcium concentration slightly below normal (i.e., < 0.5 mg/dL below normal) or normal; maintain the calcium-phosphate product < 5.5 mg²/dL² (4.4 mmol²/L²); avoid hypercalciuria; avoid hypercalcemia; and avoid renal (nephrocalcinosis/nephrolithiasis) and other extraskeletal calcifications. 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} Natpara therapy is noted as a useful therapeutic option, particularly in patients who require large amounts of calcium and vitamin D for control and those who cannot be controlled, despite receiving large supplemental therapy.

The European Society of Endocrinology (ESE) published clinical guidelines for the treatment of chronic hypoparathyroidism in adults in 2015.¹² The ESE notes the aim of treatment is to relieve symptoms of hypocalcemia and improve the patient's quality of life. The standard of care includes oral calcium salts and vitamin D metabolites. Although the ESE notes that Natpara seems to be an attractive option for patients who are unstable and who cannot safely maintain their serum and urinary calcium in the target range, the ESE notes the lack of long-term data for Natpara.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Natpara. 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 efficacy, approval requires Natpara to be prescribed by, or in consultation with, a physician who specializes in the condition being treated. All approvals are provided for the duration noted below.

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.** The patient cannot be well-controlled on calcium supplements and active forms of vitamin D alone; AND
 - ii.** The patient's 25-hydroxyvitamin D stores are sufficient (before initiating Natpara therapy) per the prescribing physician; AND
 - iii.** The 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.** The patient cannot be well-controlled on calcium supplements and active forms of vitamin D alone; AND
 - ii.** The patient's 25-hydroxyvitamin D stores are sufficient (during Natpara therapy) per the prescribing physician; AND
 - iii.** The 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), as determined by the prescriber.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Natpara has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

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

REFERENCES

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HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual Revision	Extended approval for initial therapy from 1 year to 3 years. Added criteria to address Natpara for patients who are currently receiving Natpara and who are responding to Natpara therapy (3 year approval).	04/13/2016
Annual Revision	No criteria changes.	04/19/2017
Annual revision	No criteria changes.	04/25/2018
Annual Revision	No criteria changes.	04/17/2019

TAC – Therapeutic Assessment Committee; * For a further summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>.