MEDICAL MUTUAL®

Drug Policy

Policy:	Natpara (parathyroid hormone)	Annual Review Date: 07/18/2024 Last Revised Date: 07/18/2024

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. There are several limitations to Natpara use: it is only recommended 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. Natpara was studied in one randomized, double-blind, placebo-controlled pivotal study. The primary endpoint was the proportion of patients who achieved all three criteria for the composite endpoint at Week 24: ≥ 50% reduction in the oral calcium dose (from baseline), ≥ 50% reduction in the oral active vitamin D dose (from baseline), and maintenance of a stable albumin-corrected total serum calcium concentration ≥ baseline concentration and ≤ the upper limit of normal, but ideally within the target range of 2.0 to 2.25 mmol/L (8 mg/dL to 9 mg/dL). At Week 24, significantly more patients in the Natpara group achieved the primary endpoint compared with placebo: 53% vs. 2%, respectively ($P < 0.0001$).

REMS Program

Because of the potential risk of osteosarcoma associated with Natpara therapy, Natpara is available only through a restricted REMS program called the Natpara REMS Program. Under the Natpara REMS Program, only certified healthcare providers can prescribe, and only certified pharmacies can dispense Natpara. Further information is available at www.NATPARAREMS.com or by telephone at 1-855-NATPARA.

POLICY STATEMENT

This policy involves the use of Natpara. Prior authorization is recommended for pharmacy benefit coverage of Natpara. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

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 be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

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RECOMMENDED AUTHORIZATION CRITERIA

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

1. **Chronic Hypoparathyroidism, Initial Therapy**
   Criteria. *Patient must meet the following criteria (A, B, C, D and E):*
   - **A.** Not well-controlled on calcium supplements and active forms of vitamin D alone; AND
   - **B.** 25-hydroxyvitamin D stores are sufficient (before initiating Natpara therapy) per the prescribing physician; AND
   - **C.** Serum calcium concentration is > 7.5 mg/dL before initiating Natpara therapy; AND
   - **D.** Prescribed by or in consultation with an endocrinologist; AND
   - **E.** Patient is aged 18 years or older.

2. **Chronic Hypoparathyroidism, Patient is currently Receiving Therapy**
   Criteria. *Patient must meet the following criteria (A and B):*
   - A. Serum calcium and 25-hydroxyvitamin D stores are sufficient (during Natpara therapy) per the prescribing physician; AND
   - B. 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.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 365 days
B) *Extended Approval:* 365 days

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. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Patients with acute post-surgical hypoparathyroidism.** Natpara was only studied in patients with chronic hypoparathyroidism.

2. **Patients with hypoparathyroidism caused by calcium-sensing receptor mutations.** Natpara was not studied in this patient population.

3. **Patients with an increased baseline risk of osteosarcoma.** Natpara causes an increased incidence of osteosarcoma. Avoid use in patients with a history of Paget disease of bone or unexplained elevations of alkaline phosphate, open epiphyses in young adults, hereditary disorders predisposed to osteosarcoma and/or prior history of external beam or implant radiation involving the skeleton.

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

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Natpara® [prescribing information]. Bedminster, NJ: NPS Pharmaceuticals; July 2020 .
2. Mannstad M, Clarke BL, Vokes T, et al. Efficacy and safety of recombinant human parathyroid hormone (I-84) in hypoparathyroidism (REPLACE): a double-blind, placebo-controlled, randomised, phase 3 study. *Lancet Diabetes Endocrinol*. 2013;1:275-283.
3. Bilezikian JP, Khan A, Potts JT Jr, et al. Hypoparathyroidism in the adult: epidemiology, diagnosis, pathophysiology, target-organ involvement, treatment, and challenges for future research. *J Bone Mineral Res*. 2011;26(10):2317-2337.
4. Cusano NE, Rubin MR, Sliney J Jr, Bilezikian JP. Mini-review: new therapeutic options in hypoparathyroidism. *Endocrine*. 2012;41(3):410-414.
5. Powers J, Joy K, Ruscio A. Prevalence and incidence of hypoparathyroidism in the USA using a large claims database. *J Bone Mineral Res*. 2013;28(12):2570-2576.
6. Shoback D. Clinical practice. Hypoparathyroidism. Review. *N Engl J Med*. 2008;359(4):391-403.
7. DeSanctis V, Soliman A, Fiscina B. Hypoparathyroidism: from diagnosis to treatment. *Curr Opin Endocrinol Diabetes Obes*. 2012;19:435-442.
8. Rejnmark L, Underbjerg L, Sikjaer T. Therapy of hypoparathyroidism by replacement with parathyroid hormone. *Scientifica (Cairo)*. 2014;2014:765629. Epub 2014 Jul 1.
9. Rubin MR, Dempster DW, Zhou H, et al. Dynamic and structural properties of the skeleton in hypoparathyroidism. *J Bone Mineral Res*. 2008;23(12):2018-2024.
10. Ramakrishnan Y, Cocks HC. Impact of recombinant PTH on management of hypoparathyroidism: a systematic review. *Eur Arch Otorhinolaryngol*. 2016;273(4):827-835.
11. Bollerslev J, Rejnmark L, Marcocci C, et al. European Society of Endocrinology clinical guideline: treatment of chronic hypoparathyroidism in adults. *Eur J Endocrinol*. 2015;173:G1-G20.
12. Parathyroid Hormone. In: DRUGDEX [online database]. Truven Health Analytics; Greenwood Village, CO. Last updated 5 Feb 2018. Accessed on 10 July 2018.
13. Brandi M, Bilezikian J, Shoback D, et al. Management of Hypoparathyroidism: Summary Statement and Guidelines, *The Journal of Clinical Endocrinology & Metabolism* 2016;101(6):2273–2283.