Clinical Policy Title:	parathyroid hormone
Policy Number:	RxA.244
Drug(s) Applied:	Natpara®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Parathyroid hormone (Natpara®) is a parathyroid hormone. It is indicated as an adjunct to calcium and vitamin D to control hypocalcemia in patients with hypoparathyroidism.

Limitation(s) of 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.
- Natpara® was not studied in patients with hypoparathyroidism caused by calcium-sensing receptor mutations and in patients with acute post-surgical hypoparathyroidism.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
parathyroid Hormone (Natpara®)	Hypocalcemia secondary to hypoparathyroidism	50 mcg Subcutaneous once daily; increase in increments of 25 mcg every 4 weeks.	100 mcg/day

Dosage Forms

- Multiple-dose, dual-chamber glass cartridges: 25 mcg/dose, 50 mcg/dose, 75 mcg/dose and 100 mcg/dose

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the term of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Hypocalcemia Secondary to Hypoparathyroidism (must meet all):

1. Diagnosis of hypocalcemia secondary to hypoparathyroidism;
2. Prescribed by or in consultation with an endocrinologist;
3. Age ≥ 18 years;
4. Natpara® is prescribed as an adjunct to calcium supplements and active forms of vitamin D, unless

contraindicated;
5. Recent (dated within the last 30 days) serum calcium level is > 7.5 mg/dL;
6. Recent (dated within the last 30 days) lab result shows sufficient 25-hydroxyvitamin D stores [≥ 50 nmol/L (≥ 20 ng/mL)];
7. Failure of a 12-week trial of calcium supplements and active forms of vitamin D (e.g., calcitriol) at up to maximally indicated doses, unless contraindicated or clinically significant adverse events are experienced;
   **Prescriber must indicate that the hypocalcemia is not well controlled with calcium supplements and active forms of vitamin D (see examples in Appendix B below).*
8. Dose does not exceed 100 mcg per day.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Hypocalcemia Secondary to Hypoparathyroidism (must meet all):
1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy as evidenced by one of the following (a or b):
   a. Recent (dated within the last 90 days) serum calcium level is within 8-9 mg/dL;
   b. Recent serum calcium level is > 9 mg/dL, and Natpara® dose is being decreased;
3. If request is for a dose increase, new dose does not exceed 100 mcg per day.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
calcitriol (Rocaltrol®)	0.25 mcg by mouth once daily initially. Dose may be increased at 2- to 4-week intervals	2 mcg/day
calcium carbonate (Caltrate®,OsCal®, Tums®)	1-3 g by mouth once daily in divided doses	3 g/day
calcium citrate (Cal-Citrate®)	1-3 g by mouth once daily in divided doses	3 g/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

APPENDIX C: Contraindications/Boxed Warnings
- Contraindication(s):

- Hypersensitivity to any component of the product

- Boxed Warning(s):
  - Potential risk of osteosarcoma.
    - In male and female rats, parathyroid hormone caused an increase in the incidence of osteosarcoma (a malignant bone tumor) that was dependent on dose and treatment duration. A risk to humans could not be excluded.
    - Because of the potential risk of osteosarcoma, prescribe Natpara® only to patients who cannot be well-controlled on calcium and active forms of vitamin D and for whom the potential benefits are considered to outweigh the potential risk.
    - Avoid use of Natpara® in patients who are at increased baseline risk for osteosarcoma (including those with Paget's disease of bone or unexplained elevations of alkaline phosphatase, pediatric and young adult patients with open piphyses, patients with hereditary disorders predisposing to osteosarcoma or patients with a history of prior external beam or implant radiation therapy involving the skeleton).
    - Natpara® is available only through a restricted program called the Natpara® REMS Program.

APPENDIX D: General Information

- As stated in the prescribing information, the prescriber should confirm 25- hydroxyvitamin stores are sufficient and serum calcium is above 7.5 mg/dL before starting Natpara®.
- The goal of Natpara® treatment is to achieve serum calcium within the lower half of the normal range (8 to 9 mg/dL) and to reduce the required doses of calcium and vitamin D supplementation.
- Examples of a "failure" of calcium and vitamin D supplementation can include: large swings in calcium levels, calcium phosphate product cannot be maintained within an acceptable range, high risk of renal complications due to hypercalciuria or calcium containing stones, evidence of renal complications such as nephrolithiasis or having a condition causing poor calcium and vitamin D absorption.

References

1. Natpara® Prescribing Information. Lexington, MA: Shire-NPS Pharmaceuticals, Inc.; July 2020. Available at: www.Natpara®.com. Accessed March 10, 2021.
2. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed March 10, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Clinical Policy Title was updated. 2. Drug(s) Applied was updated. 3. Line of Business Policy Applies to was update to all lines of business. 4. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been by RxAdvance..."	07/23/2020	09/14/2020

5. Initial Approval criteria: Commercial and Medicaid approval duration were updated from member's renewal date to 6 months. 6. Continued Approval criteria: Commercial and Medicaid approval duration were updated from member's renewal date to 6 months. 7. References were updated. 8. APPENDIX C was updated to include detailed Boxed warning of Potential risk of osteosarcoma. 9. APPENDIX B: Therapeutic Alternatives was updated to exclude Cal-C-Caps® because this product is not available.		
Policy was reviewed: 1. Abbreviated forms updated to full forms. 2. Appendix B: Therapeutic alternative verbiage changed to “Below are suggested…”. 3. References were reviewed and updated.	03/10/2021	06/10/2021