Drug Monograph

Drug/Drug Class:	**Natpara™ (parathyroid hormone) injection/ Parathyroid Hormone**
Prepared for:	MO HealthNet
Prepared by:	Xerox Heritage, LLC

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose:	The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use.
Dosage Forms & Manufacturer:	Natpara™ is supplied as a multiple dose, dual-chamber glass cartridge containing a sterile powder and diluent in 4 dosage strengths. It is available as 25 mcg per dose, 50 mcg per dose, 75 mcg per dose, and 100 mcg per dose of parathyroid hormone. NPS Pharmaceuticals, Inc. Bedminster, NJ 07921
Summary of Findings:	Natpara demonstrated efficacy in the treatment of hypocalcemia in patients with hypoparathyroidism in the randomized, double-blind, placebo-controlled, phase 3 REPLACE trial. Significantly more patients who received Natpara achieved a 50% reduction from baseline in the daily dose of active vitamin D and calcium, plus an albumin-corrected serum calcium level between the baseline level and the ULN, compared with placebo (53% vs 2%). Among patients who received Natpara, 43% were able to discontinue active vitamin D and take supplemental calcium doses of 500 mg/day or less, compared with 5% who received placebo.
Status Recommendation:	☐ Prior Authorization (PA) Required ☐ Open Access ☒ Clinical Edit ☐ PDL
Type of PA Criteria:	☐ Increased Risk of ADE ☐ Preferred Agent ☒ Appropriate Indications ☐ Under Solicitation

Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payors are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction[3]

Hypoparathyroidism is an uncommon condition in which your body secretes abnormally low levels of parathyroid hormone (PTH). PTH plays a key role in regulating and maintaining a balance of your body's levels of two minerals — calcium and phosphorus. The low production of PTH in hypoparathyroidism leads to abnormally low ionized calcium levels in your blood and bones and to an increase of serum phosphorus.

Dosage Form(s) [1]

Natpara™ is supplied as a multiple dose, dual-chamber glass cartridge containing a sterile powder and diluent in 4 dosage strengths. It is available as 25 mcg per dose, 50 mcg per dose, 75 mcg per dose, and 100 mcg per dose of parathyroid hormone.

Manufacturer [1]

NPS Pharmaceuticals, Inc., Bedminster, NJ 07921

Indication(s) [1]

Natpara™ is indicated as an adjunct to calcium and vitamin D to treat hypocalcemia in patients with hypoparathyroidism.

Clinical Efficacy [1,2] (mechanism of action/pharmacology, comparative efficacy)

Natpara™ raises serum calcium levels through increased absorption in the intestines, increased reabsorption at the renal tubules, and increased bone turnover.

Pharmacokinetics

	Natpara
Volume of distribution	5.35 L
Metabolism	Liver via cleavage by cathepsins
Excretion	Urine
Half-life	2.83 to 3.02 hours

Natpara was more effective than placebo in improving serum calcium levels and reducing doses of active vitamin D and oral calcium therapy in patients with hypoparathyroidism.

STUDY DESIGN	Randomized, double-blind, placebo-controlled, multicenter, 24-week,

	phase 3 clinical trial (n=134).
INCLUSION CRITERIA	Adults with hypoparathyroidism for at least 18 months who were receiving active vitamin D and oral calcium treatment.
EXCLUSION CRITERIA	Patients with known activating mutation in the calcium-sensing receptor gene.
TREATMENT REGIMEN	Patients (mean age, 47.5 years; 78% female) were randomized to receive Natpara 50 mcg subQ once daily (n=90) or placebo (n=44) for 24 weeks, with titration over the first 12 weeks to a maximum dose of 100 mcg once daily.
RESULTS	Significantly more patients who received Natpara achieved a 50% reduction from baseline in the daily dose of active vitamin D and calcium, plus an albumin-corrected serum calcium level between the baseline level and the ULN, compared with placebo (53% vs 2%). Among patients who received Natpara, 43% were able to discontinue active vitamin D and take supplemental calcium doses of 500 mg/day or less, compared with 5% who received placebo.
SAFETY	The overall frequencies of adverse events and serious adverse events were similar between groups.

Contraindications [(1)]

- None

Warnings and Precautions [(1)]

- Osteosarcoma may occur; use only in patients who cannot be controlled with calcium and active forms of vitamin D alone; use only when potential benefits outweigh risks; avoid use in at risk patients; monitoring recommended.
- Severe hypercalcemia has been reported; monitoring recommended; interruption or dose reduction may be required.
- Severe hypocalcemia has been reported, typically during interruption or discontinuation of therapy; monitoring recommended.
- Antibody formation may occur.
- Concomitant use with alendronate not recommended.

Adverse Effects [(1)]

Most Common, ≥ 10%	**Natpara™ (n=84)**	**Placebo (n=40)**
Paresthesia	31%	25%

Hypocalcemia	27%	23%
Headache	25%	23%
Hypercalcemia	19%	3%
Nausea	18%	18%
Hypoesthesia	14%	10%

Drug Interactions [(1)]

- Alendronate
- Digoxin

Dosage and Administration [(1)]

The recommended initial dose is 50 mcg subQ once daily; adjust to minimum dose required to prevent hypocalcemia and hypercalciuria in 25-mcg increments every 4 weeks.

Cost

GENERIC NAME	BRAND NAME	MANUFACTURER	STRENGTH	DOSE	COST*/ MONTH
Parathyroid hormone	Natpara	NPS Pharmaceuticals	25 mcg multi-dose cartridge	25 mcg/day	$7995.84
			50 mcg multi-dose cartridge	50 mcg/day	$7995.84
			75 mcg multi-dose cartridge	75 mcg/day	$7995.84
			100 mcg multi-dose cartridge	100 mcg/day	$7995.84

* Maximum Allowable Cost

Conclusion

Natpara™ is indicated to manage hypocalcemia associated with hypoparathyroidism, as an adjunct to vitamin D and calcium. It is the first parathyroid hormone available for the treatment of this rare disorder. Natpara is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) due to the risk of osteosarcoma, and should only be used in patients who are not controlled with active vitamin D and calcium supplementation. Use has not been studied in patients with acute postsurgical hypoparathyroidism or with hypoparathyroidism due to mutations in calcium-sensing receptors. Natpara demonstrated efficacy in the randomized,

double-blind, placebo-controlled, phase 3 REPLACE trial. Significantly more patients who received Natpara achieved a 50% reduction from baseline in the daily dose of active vitamin D and calcium, plus an albumin-corrected serum calcium level between the baseline level and the ULN, compared with placebo (53% vs 2%). Among patients who received Natpara, 43% were able to discontinue active vitamin D and take supplemental calcium doses of 500 mg/day or less, compared with 5% who received placebo. The most common adverse effects are paresthesia, hypocalcemia, headache, hypercalcemia, nausea, hypoesthesia, diarrhea, vomiting, arthralgia, and pain in an extremity.

Recommendation

The Division recommends adding this drug to the current parathyroid hormone clinical edit.

References

1. Product Information: Natpara™, parathyroid hormone injection. NPS Pharmaceuticals, Inc (per manufacturer), Bedminster, NJ, 01/2015.
2. Mannstadt M, Clarke BL, Vokes T et al: Efficacy and safety of recombinant human parathyroid hormone (1-84) in hypoparathyroidism (REPLACE): a double-blind, placebo-controlled, randomised, phase 3 study. Lancet Diabetes Endocrinol 2013; 1(4):275-283.
3. Diseases and Conditions: Hypoparathyroidism. Retrieved 06/09/2015 from http://www.mayoclinic.org/diseases-conditions/hypoparathyroidism/basics/definition/con-20030780

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