Natpara (parathyroid hormone) Prior Authorization with Quantity Limit Program Summary

POLICY REVIEW CYCLE

Effective Date **Date of Origin**
3/1/2023

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Natpara® (parathyroid hormone) Subcutaneous injection	Adjunct to calcium and vitamin D to control hypocalcemia in patients with hypoparathyroidism Limitations 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. • Natpara was not studied in patients with acute post-surgical hypoparathyroidism.		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Hypoparathyroidism	Hypoparathyroidism is a rare disorder of mineral metabolism characterized by hypocalcemia and absent or deficient production of parathyroid hormone (PTH). PTH is one of the major hormones that regulates calcium along with vitamin D via direct effects on the bone and kidney and indirect effects on the gastrointestinal tract. Hypoparathyroidism occurs when there is destruction of the parathyroid glands (e.g., autoimmune, surgical), abnormal parathyroid gland development, altered regulation of PTH production, or impaired PTH action. When PTH secretion is insufficient, hypocalcemia develops. Hypocalcemia can affect the function of most organs, but in hypoparathyroidism the most obvious organ systems that become dysfunctional are neurological, cognitive, muscular, and cardiac.(2,3,5) The diagnostic biochemical hallmarks of hypoparathyroidism are hypocalcemia in association with deficient production of PTH. It is thus readily distinguished from pseudohypoparathyroidism, a genetic disorder of PTH resistance in which the circulating PTH concentration is elevated.(2,3) The diagnosis of hypoparathyroidism is also readily distinguished from secondary causes of hypocalcemia (e.g., vitamin D deficiency) in which the PTH level is also high. In hypoparathyroidism, circulating concentrations of active vitamin D is usually in the lower normal range.(2,3,5)

	Treatment with oral calcium supplements and active forms of vitamin D (e.g., calcitriol, cholecalciferol, ergocalciferol) are the current standard of care. Monitoring of urinary and serum calcium and serum phosphate is required weekly initially, until a stable serum calcium concentration is achieved. Thereafter, monitoring levels at 3- to 6-month intervals is sufficient. Some patients may require the addition of thiazide diuretics with or without dietary sodium restrictions to decrease urinary calcium excretion. Some patients, despite very high amounts of calcium and active vitamin D, are subject to wide swings in their serum calcium and associated symptomology. Second line therapy is recombinant human parathyroid hormone (rhPTH), which provides an additional useful therapeutic option in the management of hypoparathyroidism. Goals of therapy with rhPTH are to minimize or eliminate the use of active vitamin D, to reduce supplemental calcium to 500 mg daily, and to maintain the serum calcium in the lower range of normal.(2,3,5)
Efficacy (1,4)	Efficacy of recombinant human PTH (rhPTH) was evaluated in a 24-week, randomized, double-blind, placebo-controlled, multicenter trial (REPLACE). In this trial, patients with established hypoparathyroidism receiving calcium and active forms of vitamin D (vitamin D metabolite or analogs) were randomized to PTH (n=84) or placebo (n=40). For the efficacy analysis, patients that fulfilled three components of a three-part response criterion were considered responders. A responder was defined as an individual who had: greater than or equal to 50% reduction from baseline in the dose of active vitamin D, greater than or equal to 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. At the end of treatment, significantly more subjects treated with Natpara compared to placebo met the response criteria (54.8% and 2.5%, respectively).
Safety (1)	Natpara carries a boxed warning for potential risk of osteosarcoma. In male and female rats, rhPTH caused an increase in incidence of osteosarcoma, with occurrence dependent on rhPTH dose and treatment duration. This effect was observed at rhPTH levels from 3 to 71 times the exposure levels in humans receiving a 100 mcg dose of rhPTH. Data could not exclude a risk to humans. Due to risk of osteosarcoma, rhPTH should be used only in patients who cannot be well-controlled on calcium and active vitamin D alone and for whom potential benefits outweigh risks. Avoid use in patients at increased baseline risk for osteosarcoma (e.g., Paget's disease of bone, elevated alkaline phosphatase, pediatric and young adult patients with open epiphyses, hereditary disorders predisposing to osteosarcoma, or history of external beam or implant radiation therapy involving the skeleton). Because of this risk, rhPTH is available only through the Natpara REMS Program. Natpara is contraindicated in patients with a known hypersensitivity to any component of the product. Co-administration of alendronate and Natpara leads to reduction in the calcium-sparing effect, which can interfere with the normalization of serum calcium. Concomitant use of Natpara with alendronate is not recommended.

REFERENCES

Number	Reference
1	Natpara prescribing information. Shire-NPS Pharmaceuticals, Inc. April 2022.
2	Brandi ML, Bilezikian JP, Shoback D, et al. Management of Hypoparathyroidism: Summary Statement and Guidelines. J Clin Endocrinol Metab 2016;101(6):2273-2283.
3	Sinnott BP. Hypoparathyroidism – Review of the Literature. J Rare Disord Diagn Ther 2018;4(3):1-7.
4	Clarke BL, Vokes TJ, Bilezikian JP, et al. Effects of Parathyroid Hormone rhPTH(1-84) on Phosphate Homeostasis and Vitamin D Metabolism in Hypoparathyroidism: REPLACE Phase 3 Study. Endocrine 2017;55(1):273-282.
5	Bilezikian JP. Hypoparathyroidism: Mini Review. J Clin Endocrinol Metab 2020;105(6):1-15.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Preferred Status	Effective Date
Natpara	parathyroid hormone (recombinant) for inj cartridge	100 MCG ; 25 MCG ; 50 MCG ; 75 MCG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Days Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist	Effective Date
Natpara	parathyroid hormone (recombinant) for inj cartridge	100 MCG ; 25 MCG ; 50 MCG ; 75 MCG	2.0	CARTS	28	Days				

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Natpara	parathyroid hormone (recombinant) for inj cartridge	100 MCG ; 25 MCG ; 50 MCG ; 75 MCG	Commercial ; HIM ; ResultsRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Natpara	parathyroid hormone (recombinant) for inj cartridge	100 MCG ; 25 MCG ; 50 MCG ; 75 MCG	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent** will be approved when ALL of the following are met: 1. ONE of the following: A. The patient has a diagnosis of hypocalcemia associated with hypoparathyroidism AND ALL of the following: 1. The patient has baseline (prior to therapy with the requested agent) vitamin D levels above the lower limit of normal **AND** 2. The patient has baseline (prior to therapy with the requested agent) serum calcium levels above 7.5 mg/dL **AND** 3. The patient has tried and had an inadequate response to maximally tolerated calcium AND vitamin D supplements (e.g., calcitriol, ergocalciferol, cholecalciferol) **AND** 4. The patient will continue calcium and vitamin D supplementation with the requested agent **AND** 5. The patient does NOT have hypoparathyroidism caused by calcium-sensing receptor (CaSR) mutations **AND**

Module	Clinical Criteria for Approval
	6. The patient does NOT have acute post-surgical hypoparathyroidism **AND** 7. The patient does NOT have pseudohypoparathyroidism **OR** B. The patient has another FDA approved indication for the requested agent **AND** 2. The patient is NOT at increased risk for osteosarcoma (e.g., Paget's disease of bone, unexplained elevations of alkaline phosphatase, hereditary disorders predisposing to osteosarcoma, history of external beam or implant radiation therapy involving the skeleton, pediatric and young adult patients with open epiphyses) **AND** 3. The patient will NOT be using the requested agent in combination with alendronate **AND** 4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., endocrinologist, nephrologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 6 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria section below. **Renewal Evaluation** **Target Agent** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND** 2. ONE of the following: A. If the patient has a diagnosis of hypocalcemia associated with hypoparathyroidism, then ALL of the following: 1. The patient has had at least a 50% reduction from baseline (prior to therapy with the requested agent) in the dose of calcium supplementation **AND** 2. The patient has had at least a 50% reduction from baseline (prior to therapy with the requested agent) in the dose of vitamin D supplementation **AND** 3. The patient has an albumin-corrected total serum calcium concentration between 8 mg/dL and 9 mg/dL **AND** 4. The patient will continue calcium supplementation with the requested agent **OR** B. If the patient has another FDA approved indication for the requested agent, the patient has had clinical benefit with the requested agent **AND** 3. The patient is NOT at increased risk for osteosarcoma (e.g., Paget's disease of bone, unexplained elevations of alkaline phosphatase, hereditary disorders predisposing to osteosarcoma, history of external beam or implant radiation therapy involving the skeleton, pediatric and young adult patients with open epiphyses) **AND** 4. The patient will NOT be using the requested agent in combination with alendronate **AND** 5. The prescriber is a specialist in the area of the patient's diagnosis (e.g., endocrinologist, nephrologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 6. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria section below.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL with PA	**Quantity Limit for the Target Agent(s)** will be approved when ONE of the following is met:

Module	Clinical Criteria for Approval
	1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **OR** 3. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication **AND** C. The prescriber has provided information in support of therapy with a higher dose for the requested indication **Length of Approval**: Initial: 6 months; Renewal: 12 months