Date: November 16th, 2020

Dear Valued Patient,

We are writing to provide an update on the information we provided in October 2020 regarding the potential for a near-term supply interruption of NATPARA® (parathyroid hormone) for Injection that may impact U.S. patients receiving NATPARA 100-mcg through the Special Use Program. We are also notifying you that we are now anticipating a near-term supply interruption of NATPARA 25-mcg, as well.

As we communicated in October, we have been monitoring supply of NATPARA to prepare for potential supply interruptions. Based on our current assessments, we are anticipating supply interruptions for NATPARA 25-mcg, as early as **December 8, 2020**, as well as NATPARA 100-mcg as early as **January 2, 2021**.

If you are receiving NATPARA 25-mcg or NATPARA 100-mcg, please see the following time-sensitive information regarding the immediate actions you must take. If you are receiving other doses of NATPARA, there's nothing you need to do at this time. However, supply status updates for all other NATPARA doses are also included in this letter.

IMMEDIATE ACTION REQUIRED FOR PATIENTS RECEIVING NATPARA 25-MCG OR NATPARA 100-MCG
If you have not yet contacted your prescribing physician to determine the best treatment plan for you, please contact him/her as soon as possible. NATPARA 25-mcg is expected to be unavailable due to a supply interruption as soon as December 8, 2020, and NATPARA 100-mcg is expected to be unavailable due to a supply interruption as soon as January 2, 2021. Based on your prescriber's independent medical judgement, your revised treatment plan may require a new prescription. Please ensure you work closely with your prescribing physician on any changes to your treatment plan, including the potential for a new prescription.

Patient safety is Takeda's main priority and, as a patient enrolled in the Single Use Program who is receiving **NATPARA 25-mcg** or **NATPARA 100-mcg**, we are alerting you and your prescribing physician that any potential interruption or reduction in the daily dose of NATPARA can cause a sharp decrease in blood calcium levels (severe hypocalcemia) which can be dangerous. It is important for you to work closely with your healthcare provider for important medical recommendations, including frequent monitoring of your blood calcium levels and close titration of active vitamin D and calcium supplements if you stop or alter your dose as a result of this supply interruption to avoid hypocalcemia.

NO IMMEDIATE ACTION REQUIRED FOR PATIENTS RECEIVING NATPARA 50-mcg or NATPARA 75-mcg:
At this time, we do not anticipate near-term supply interruptions for **NATPARA 50-mcg** or **NATPARA 75-mcg** doses before the end of 2020. However, we are closely monitoring these NATPARA doses and could experience supply interruptions in the event that manufacturing disruptions persist. We are committed to supply continuity and will provide you and your prescribing physician with an update on all NATPARA doses by mid-December.

Compliance with Special Use Program Terms & Conditions
As a patient who is receiving NATPARA through the Special Use Program, we want to remind you that each NATPARA cartridge under the Special Use Program (single dose use) is intended for one use only,

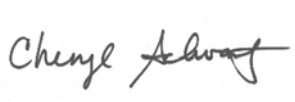
and that used cartridges with remaining product are to be returned to Takeda in accordance with the Special Use Program (single dose use) instructions. Non-compliance with the rules under the Special Use Program (single dose use) could result in termination of your ability to receive NATPARA product through the program.

OnePath will continue to work closely with your prescribing physician to support your treatment plan. If you have any immediate questions or concerns, please contact your Takeda OnePath® Patient Support Manager at 866-888-0660. Patient Support Managers are available Monday through Friday 8:30 AM – 8:00 PM ET.

Enclosed for your reference is the full NATPARA Prescribing Information and Medication Guide. For additional medical information, please contact your healthcare provider.

We recognize the important medical need that NATPARA fills for patients like you who are living with chronic hypoparathyroidism. While we focus on limiting these supply interruptions for patients who are receiving NATPARA through the Special Use Program, we continue to prioritize the goal of safely bringing NATPARA back to the broader patient community with U.S. Regulatory Authority oversight.

Sincerely,



Cheryl Schwartz
Head of U.S. Rare Disease Business Unit

Daniel McNamara
Head of U.S. Patient Services

What is NATPARA® (parathyroid hormone) for Injection?

- NATPARA is a prescription parathyroid hormone used with calcium and vitamin D to control low blood calcium (hypocalcemia) in people with low parathyroid hormone blood levels (hypoparathyroidism).
- NATPARA is only for people who do not respond well to treatment with calcium and active forms of vitamin D alone, because it may increase the possible risk of bone cancer (osteosarcoma).
- NATPARA was not studied in people with hypoparathyroidism caused by calcium-sensing receptor mutations.
- NATPARA was not studied in people who get sudden hypoparathyroidism after surgery.
- It is not known if NATPARA is safe and effective for children 18 years of age and younger. NATPARA should not be used in children and young adults whose bones are still growing.

Important Safety Information
What is the most important information I should know about NATPARA?
Warning: Possible bone cancer (osteosarcoma).

- During animal drug testing, NATPARA caused some rats to develop a bone cancer called osteosarcoma. It is not known if people who take NATPARA will have a higher chance of getting osteosarcoma. Tell your doctor right away if you have pain in any areas of your body that does not go away, or any new or unusual lumps or swelling under your skin that is tender to touch.

- **NATPARA is only available through the NATPARA Risk Evaluation and Mitigation Strategy (REMS) Program.** The purpose of the NATPARA REMS program is to inform patients about the potential risk of osteosarcoma associated with the use of NATPARA. For more information about this REMS program, call 1-855-NATPARA (628-7272) or go to **www.NATPARAREMS.com.**

NATPARA may cause other serious side effects, including:

High blood calcium (hypercalcemia)

- NATPARA can cause some people to have a higher blood calcium level than normal.

1. Your doctor should check your blood calcium before you start and during your treatment with NATPARA.
2. Tell your doctor if you have nausea, vomiting, constipation, low energy, or muscle weakness. These may be signs that you have too much calcium in your blood.

Low blood calcium (hypocalcemia)

- People who stop using or miss a dose of NATPARA may have an increased risk of severe low blood calcium levels.
- Tell your doctor if you have tingling of your lips, tongue, fingers and feet, twitching of face muscles, cramping of feet and hands, seizures, depression, or have problems thinking or remembering.

Who should not use NATPARA?

- **Do not use NATPARA** if you are allergic to parathyroid hormone or any of the ingredients in NATPARA.

What should I tell my healthcare provider before using NATPARA?

- **Before you start using NATPARA, tell your doctor about all of your medical conditions. Tell your doctor about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

What are the possible side effects of NATPARA?

- **NATPARA may cause serious side effects like allergic (hypersensitivity) reaction, including anaphylaxis**. Tell your healthcare provider or get emergency medical help right away if you have any of the following symptoms of an allergic reaction:
  - swelling of your face, lips, mouth, or tongue
  - breathing problems
  - fainting, dizziness, feeling lightheaded (low blood pressure)
  - fast heartbeat
  - itching
  - rash
  - hives

- **The most common side effects of NATPARA include:** tingling, tickling, or burning feeling of the skin, low or high blood calcium, headache, nausea, reduced sense of touch or sensation, diarrhea, vomiting, pain in joints, too much calcium in urine, and pain in limbs.

Enclosure: NATPARA Full Prescribing Information