October 20, 2020

Dear Hypoparathyroidism Association board members and community,

On behalf of Takeda, we wanted to share a product supply-related update that may impact patients receiving the 100-mcg dose of NATPARA® (parathyroid hormone) through the Special Use Program ("SUP").

We are informing U.S. healthcare providers and all patients receiving NATPARA through the Special Use Program of the potential for a near-term supply interruption of **NATPARA 100-mcg** as early as November 21, 2020. The anticipated supply interruption does not affect patients outside of the U.S.

The anticipated supply interruption is related to unexpected manufacturing disruptions that are separate from the issue of rubber particulates originating from the rubber septum of the NATPARA cartridge that led to the U.S. recall in September 2019. We deeply regret that we are anticipating an interruption in supply and are making it a priority to bring product back quickly. At the same time, we are working on possible options for alternate treatment approaches with U.S. Regulatory Authority (U.S. Food & Drug Administration or "FDA") oversight and will keep all impacted patients and their prescribing physicians informed.

While other NATPARA doses are not expected to be impacted at this time, we are closely monitoring the remaining NATPARA doses (25-mcg, 50-mcg and 75-mcg), which could experience supply interruptions if manufacturing disruptions persist and will provide SUP-enrolled patients and their prescribing physicians with a supply update no later than November 16, 2020.

With patient safety as Takeda's main priority, we are alerting impacted patients and their healthcare providers 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. Specifically, we are emphasizing to impacted patients the importance of working closely with their prescribing physician for important medical recommendations, including frequent monitoring of blood calcium levels and close titration of active vitamin D and calcium supplements if the patient's NATPARA is stopped or the dose is altered (e.g., as a result of supply interruption) to avoid hypocalcemia.

If you are a patient receiving NATPARA 100-mcg, a Takeda OnePath representative will also be reaching out to you in the coming days to walk you through this update and align on next steps. If you have any immediate questions or concerns, please call OnePath at 866-888-0660 Monday through Friday 8:30 AM – 8:00 PM ET.

We recognize the important medical need that NATPARA fills for those of you who are living with hypoparathyroidism. While we focus on restoring supply continuity for SUP-enrolled patients, we continue to work in parallel on the resupply effort to bring NATPARA back to the broader patient community with the oversight of the FDA.

Sincerely,

Cheryl Schwartz
Head of US Rare Disease Business Unit

Tom Koutsavlis
Head of US Medical Affairs

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.
  - Your doctor should check your blood calcium before you start and during your treatment with NATPARA.
  - 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.

Tell your doctor right away if you have any of these signs and symptoms of **high or low blood calcium** levels.

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.

These are not all the possible side effects of NATPARA. For more information, talk with your doctor.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit **www.fda.gov/medwatch** or call **1-800-FDA-1088**.

Please go to **https://www.shirecontent.com/PI/PDFs/Natpara_USA_ENG.pdf** **for the Full Prescribing Information and Medication Guide.**

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