



November 17, 2020

Dear Hypoparathyroidism Association board members and community,

On behalf of Takeda, we are sharing a supply-status update to the information we provided in October 2020 regarding the potential for near-term supply interruptions of NATPARA® (parathyroid hormone) for Injection that may impact U.S. patients receiving NATPARA through the Special Use Program.

As we communicated in October, we have been monitoring supply of NATPARA to prepare for potential supply interruptions. Since our initial supply update, the manufacturing disruptions have also impacted the 25-mcg dose of NATPARA. 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**.

As a reminder, the anticipated supply interruptions are 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 we are working with urgency to maintain supply continuity.


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 maintaining supply continuity and will provide impacted patients and their healthcare prescribers with an update on all NATPARA doses by mid-December.

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 25-mcg or NATPARA 100-mcg, a Takeda OnePath® Patient Support Manager will also be reaching out to you to walk you through this update and align on next steps. If you have any immediate questions or concerns, OnePath® Patient Support Managers are available 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 patients enrolled in the Special Use Program, we continue to work in parallel on the effort to resupply NATPARA to the broader patient community with the oversight of the FDA. As we shared in October, we expect to be able to provide an update on the timeline to bring back NATPARA by the end of March 2021.

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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