March 31, 2021

Dear Valued Patient,

On behalf of Takeda, we are sharing the following NATPARA® (parathyroid hormone) for Injection information regarding the status of the NATPARA recall in the U.S.

As a patient previously prescribed NATPARA, we know that you are eager for an update about our plans to make NATPARA available again for appropriate patients with chronic hypoparathyroidism in the U.S. While we have made progress on the original issue that led to the U.S. recall, which was the issue of rubber particulates originating from the rubber septum of the NATPARA cartridge, we have not yet reached a resolution. We continue to face complex challenges in bringing NATPARA back to the broader patient community in the U.S.

We are currently experiencing a manufacturing delay that is 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. This manufacturing delay has further impacted our timelines, and at this time we do not expect a return to the U.S. market before March 31, 2022.

We recognize that this update may be difficult for those who have been eagerly awaiting information about our anticipated timelines for bringing NATPARA back. We are also disappointed that there is not better news to share with you. We encourage you to continue working with your health care team to determine how to best manage your condition during this extended period without NATPARA.

We plan to schedule a teleconference with the U.S. chronic hypoparathyroidism patient community in the coming weeks. Please watch for more information about that upcoming event in the NATPARA Updates section of our Takeda U.S. Newsroom at https://www.takeda.com/en-us/newsroom/natpara-updates/. Information should be posted during the week of April 5, 2021. We will also share the information with the Hypoparathyroidism Association.

Sincerely,

Cheryl Schwartz  Rick Ascroft
Head of U.S. Rare Disease Business Unit       Senior Vice President, Patient Services & Managed Markets
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.
  - 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

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
muscle weakness. These may be signs that you have too much calcium in your blood.

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

- 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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