January 21, 2020

Dear Valued Patient,

On behalf of Takeda, I am writing to update you about the status of NATPARA in the US. We have worked closely with the Food and Drug Administration (FDA) over the last several months on our proposed plan to bring NATPARA back to patients. Based on data generated from additional testing and feedback from the FDA, it is now clear that additional product modifications and testing will be required that will significantly impact our timelines. While we are continuing to work toward resupply as quickly as possible, I am disappointed to share that the additional testing and potential device modifications will likely cause more than a year's delay in bringing NATPARA back to US patients. We deeply regret this difficult news. Additional work is ongoing with the FDA, and we will continue to keep you informed as new information becomes available.

While we continue this critically important work, we are also committed to ensuring supply, through the Special Use Program, to patients previously prescribed NATPARA who are at extreme risk of life-threatening complications as a result of discontinuation of treatment. To date, 358 patients are receiving NATPARA at no cost as part of the Program, which was developed in collaboration with the FDA.

We understand that the Special Use Program is extremely limited and will not address the broader needs of patients who were previously prescribed NATPARA. As we have communicated previously, the Special Use Program requires that product usage be limited to a single dose per cartridge, instead of 14 doses per cartridge, to minimize the potential of particle formation caused by repeat punctures. This means that patients enrolled in the Special Use Program use one year's worth of cartridges each month. Because of this, we must limit the Program to patients who are at significant risk of life-threatening complications to ensure supply for the most high-risk patients.

We know that this is not the news you were hoping to hear, and we recognize how difficult this interruption in therapy has been for you and your families. Our top priority, and our commitment to you all, is to continue to work with the FDA to identify all potential options for getting this critical medication back to you as quickly and as safely as we can.

Sincerely,

Cheryl Schwartz
Head of US Hematology & Rare Disease Business Unit

Shire-NPS Pharmaceuticals, Inc., part of the Takeda Group
300 Shire Way
Lexington, MA 02421
USA

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 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.**

S53483 01/20

NPS Pharmaceuticals, Inc., part of the Takeda Group
300 Shire Way
Lexington, MA 02421
USA