US Recall of NATPARA® (parathyroid hormone) for Injection

IMPORTANT INFORMATION FOR NATPARA PATIENTS

Dear Valued Patient,

The purpose of this letter is to share some new and important information regarding Takeda's September 5, 2019 US recall for all doses of NATPARA® (parathyroid hormone) for Injection (25 mcg, 50 mcg, 75 mcg, and 100 mcg).

NATPARA is a parathyroid hormone currently approved in the US as the only adjunctive treatment for adult patients with chronic hypoparathyroidism who cannot be adequately controlled with standard therapy alone (calcium and vitamin D).

On October 2nd, the US Food & Drug Administration ("US FDA") informed Takeda that, following further review of the NATPARA recall, they are classifying NATPARA recall as Class I due to the potential risk of rubber stopper particles clogging the needle and leading to under-dosing. The Class I recall requires that all patients with product received prior to the recall of September 5, 2019 ("Recalled Product") return their unused NATPARA to Takeda to prevent the use of Recalled Product. The safety profile of NATPARA remains consistent with the product label.

In parallel, Takeda continues to work closely with the US FDA regarding NATPARA, and values the US FDA's collaboration and feedback as we work together to resupply NATPARA to patients who need it.

Based on the FDA's classification, enclosed in this envelope you will find information from Stericycle, a third-party vendor that works with companies such as Takeda to coordinate product recalls. This includes instructions on how to return your unused NATPARA product using the Patient Return Kit.

With patient safety as the company's main priority, Takeda is communicating directly with healthcare professionals, patients, and specialty pharmacies in the US regarding the actions required as a result of the Class 1 recall. Consistent with the product labelling, Takeda is alerting NATPARA patients and prescribers that discontinuing NATPARA abruptly can cause a sharp decrease in blood calcium levels (severe hypocalcemia) which can result in serious health consequences. It is critically important that patients contact their prescribing healthcare provider to discuss their individual treatment plan and ensure close supervision, including frequent monitoring of blood calcium levels and close titration of active vitamin D and calcium supplements upon stopping NATPARA to avoid low blood calcium (hypocalcemia).

It is critical to note that the Special Use Program is unaffected by the Class I recall and continues to support patients previously prescribed NATPARA who are at extreme risk of life-threatening complications as a result of discontinuation of NATPARA. This means that the

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300 Shire Way
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single-use NATPARA cartridges that you have received, or are expected to receive under the Special Use Program, are excluded from the Class I recall and you should continue to use them as prescribed by your physician.

Any patient who believes that they may qualify for the Special Use Program should contact their prescribing healthcare provider. Through this program, healthcare providers will be able to request NATPARA for extraordinary, life-threatening cases. This program requires a signed physician case report confirming the physician's decision to prescribe NATPARA and their determination that without continued access to NATPARA the patient faces life-threatening health consequences. The prescribing physician and the Medical Review committee will then determine if a patient is at extreme medical risk and should have access to NATPARA. The Medical Review committee is evaluating eligibility on a case-by-case basis for patients who are at most risk for life-threatening complications.

All of us at Takeda understand the impact that this recall has on patients like you, and we will continue to work closely with the FDA until we are able to resolve the issue and resume supply.

To contact a OnePath Patient Support Manager, please call 1-866-888-0660. OnePath is available Monday through Friday, 8:30am to 8:00pm, Eastern Time.

Sincerely,

Daniel McNamara
Head of US Patient Services
Takeda Pharmaceutical Company Limited

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

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)
  - itching
  - rash
  - hives

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- 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.**

S52402 10/19

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300 Shire Way
Lexington, MA 02421USA