Takeda Provides Year-End Update for NATPARA

[December 17, 2021] Takeda is providing a year-end update for NATPARA® (parathyroid hormone) that the FDA has acknowledged receipt of the Prior Approval Supplement (PAS) submission announced in September 2021 and the review is ongoing. The NATPARA PAS submission proposes device component changes that include a new septum and new needle. These proposed changes are intended to address the issue of rubber particulates originating from the rubber septum of the NATPARA cartridge that led to the US recall in 2019.

FDA has communicated to Takeda that this PAS submission is associated with a six-month review timeline. Once the FDA completes their review, there are two potential regulatory outcomes of FDA's review: 1) FDA approval of the PAS, or 2) regulatory feedback that may require significant changes to our proposed approach, or lead to a revised approach. If the FDA requests additional data or alternative proposals during or at the end of the review process, a new submission will be required, and the review/approval timelines will be extended.

While the NATPARA PAS submission represents an important step to address the original issue that led to the US recall, the manufacturing and supply issue that the Company has previously shared will also impact the timeline for bringing NATPARA back in the US. At this time, those issues remain complex.

Given the serious risks associated with abrupt discontinuation of NATPARA, the Company would not bring NATPARA back to the broader US hypoparathyroidism patient population without being able to ensure reliable and consistent supply. Takeda continues to work with urgency to test and evaluate approaches to best address these complex manufacturing and supply issues. Patients who are enrolled in the Special Use Program (SUP) continue to have access to NATPARA through that program.

All of us at Takeda remain committed to keeping the hypoparathyroidism community informed in the coming months and will provide another regulatory status update in March or April of 2022, after we hear from the FDA.

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.**

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