



April 12, 2021

Dear Hypoparathyroidism Community,

We are providing this update to share information related to the Class 1 Recall of NATPARA® (parathyroid hormone) for Injection in the US. The US Food & Drug Administration (FDA) recently posted an updated status for the US NATPARA recall on its website as part of a weekly Enforcement Report. The Enforcement Report shows a “termination date of 3/23/2021” for the NATPARA recall, as well as an updated status that now reads “terminated”.

What does the updated status mean?

The updated recall status means that the physical recalled product has been removed from the US marketplace. From that perspective, the recall of the physical product has been completed or “terminated”.

Does this mean that NATPARA will now be available to the broader US hypoparathyroidism patient community?

It is important to clarify that the updated status refers to the physical activities related to removing the recalled product from the US marketplace at the time the recall was initiated in September 2019. The underlying causes of the device issue that led to the decision to recall NATPARA must be remediated or “fixed” and the US regulatory authority (FDA) must review and approve the proposed fix in order to reintroduce the product back to the US market. As we have described previously, we have not yet resolved the device issue and we are also managing through separate issues related to supply. We continue to work hard to understand and address those issues with the goal of bringing NATPARA back.

The updated “terminated” status of the recall does not have any impact on the NATAPRA Special Use Program.

Does the word “terminated” mean that efforts to fix the problem and bring NATPARA back to the US patient population have been “terminated”?

Takeda remains committed to the hypoparathyroidism community. We continue our efforts to understand and address the underlying issues with the goal of bringing NATPARA back under US regulatory oversight.

Sincerely,

A handwritten signature in black ink, appearing to read "Tom Koutsavlis".

Tom Koutsavlis
Head of US Medical Affairs

A handwritten signature in black ink, appearing to read "Cheryl Schwartz".

Cheryl Schwartz
Head of US Rare Disease Business Unit

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:
- **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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