



News Release

Takeda Issues US Recall of NATPARA[®] (parathyroid hormone) for Injection Due to the Potential for Rubber Particulate

Patients are advised to immediately consult their healthcare providers to help ensure safe discontinuation of NATPARA treatment

Takeda is working closely with the US Food and Drug Administration (US FDA) to resolve the issue and resume supply as soon as possible

Osaka, Japan, September 6, 2019 --- Takeda Pharmaceutical Company Limited ([TSE:4502/NYSE:TAK](#)) (“Takeda”) today announced that the company is issuing a US recall for all doses of NATPARA[®] (parathyroid hormone) for Injection (25 mcg, 50 mcg, 75 mcg, and 100 mcg). This recall is being conducted after discussions with the FDA and is effective immediately due to a potential issue related to rubber particulates originating from the rubber septum of the NATPARA cartridge. During the 14-day NATPARA treatment period, the septum is punctured by a needle each day to obtain the daily dosage of NATPARA solution. When the septum is repeatedly punctured, it is possible that small rubber fragments may detach into the cartridge.

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 recall. Consistent with the product labeling, 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).

The safety profile of NATPARA remains consistent with the product label. Takeda is working closely with regulatory agencies in relevant markets outside of the US where NATPAR/A is available. NATPAR/A continues to be available in these markets.

NATPARA, a recombinant human protein with the full length 84–amino–acid sequence of endogenous parathyroid hormone (PTH), is 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).

Takeda is committed to supply integrity, and we are working closely with the FDA to resolve the issue and resume supply as soon as possible. The financial impact of the recall is currently being assessed in conjunction with the remediation plan. Takeda will share the financial impact once determined.

Healthcare providers with medical-related questions or other questions about the NATPARA recall should contact Takeda Medical Information at +1-800-828-2088 and select Option 2. Patients in the US with questions about the NATPARA recall should contact OnePath at +1-866-888-0660. For full prescribing information, including warnings and precautions, please visit https://www.shirecontent.com/PI/PDFs/Natpara_USA_ENG.pdf.

Adverse reactions or quality problems experienced with the use of this product may be reported to the US FDA's MedWatch Adverse Event Reporting program either online, by regular mail or by fax.

- Complete and submit the report online: <https://www.accessdata.fda.gov/scripts/medwatch/index.cfm>
- Regular Mail or Fax: Download form www.fda.gov/MedWatch/getforms.htm, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178
- Call 1-800-332-1088 to report by phone

About NATPARA[®] (parathyroid hormone) for Injection in the US

NATPARA (parathyroid hormone) for Injection is a parathyroid hormone indicated as an adjunct to calcium and vitamin D to control hypocalcemia in patients with hypoparathyroidism.

Limitations of Use:

- Because of the potential risk of osteosarcoma, NATPARA is recommended only for patients who cannot be well-controlled on calcium supplements and active forms of vitamin D alone.
- NATPARA was not studied in patients with hypoparathyroidism caused by calcium-sensing receptor mutations.
- NATPARA was not studied in patients with acute post-surgical hypoparathyroidism.

IMPORTANT SAFETY INFORMATION

WARNING: POTENTIAL RISK OF OSTEOSARCOMA

In male and female rats, parathyroid hormone caused an increase in the incidence of osteosarcoma (a malignant bone tumor) that was dependent on dose and treatment duration. A risk to humans could not be excluded.

Because of the potential risk of osteosarcoma, prescribe NATPARA only to patients who cannot be well-controlled on calcium and active forms of vitamin D and for whom the potential benefits are considered to outweigh the potential risk.

Avoid use of NATPARA in patients who are at increased baseline risk for osteosarcoma (including those with Paget's disease of bone or unexplained elevations of alkaline phosphatase, pediatric and young adult patients with open epiphyses, patients with hereditary disorders predisposing to osteosarcoma or patients with a history of prior external beam or implant radiation therapy

involving the skeleton).

NATPARA is available only through a restricted program called the NATPARA REMS Program. For more information about the NATPARA REMS program, call 1-855-NATPARA or go to www.NATPARAREMS.com.

Contraindications:

NATPARA is contraindicated in patients with a known hypersensitivity to any component of NATPARA. Hypersensitivity reactions (e.g., anaphylaxis, angioedema, and urticaria) have occurred with NATPARA.

Warnings and Precautions:

Hypercalcemia: Severe hypercalcemia has been reported with NATPARA. The risk is highest when starting or increasing the dose of NATPARA but can occur at any time. Monitor serum calcium and patients for signs and symptoms of hypercalcemia. Treat hypercalcemia per standard practice and consider holding and/or lowering the dose of NATPARA if severe hypercalcemia occurs.

Hypocalcemia: Severe hypocalcemia has been reported in patients taking NATPARA, including cases that resulted in seizures. The risk is highest with interruption or discontinuation of NATPARA treatment but can occur at any time. Monitor serum calcium and patients for signs and symptoms of hypocalcemia, and replace calcium and vitamin D if indicated in patients interrupting or discontinuing NATPARA to prevent severe hypocalcemia.

Digoxin Toxicity: Hypercalcemia increases the risk of digoxin toxicity. In patients using NATPARA concomitantly with digoxin, monitor serum calcium more frequently and increase monitoring when initiating or adjusting NATPARA dose.

Hypersensitivity: There have been reports of hypersensitivity reactions in patients taking NATPARA. Reactions included anaphylaxis, dyspnea, angioedema, urticaria, and rash. If signs or symptoms of a serious hypersensitivity reaction occur, discontinue treatment with NATPARA, treat hypersensitivity reaction according to the standard of care, and monitor until signs and symptoms resolve. Monitor for hypocalcemia if NATPARA is discontinued.

Adverse Reactions:

The most common adverse reactions associated with NATPARA and occurring in greater than 10% of individuals were: paresthesia, hypocalcemia, headache, hypercalcemia, nausea, hypoesthesia, diarrhea, vomiting, arthralgia, hypercalciuria and pain in extremity.

Drug Interactions:

Alendronate: Co-administration of alendronate and NATPARA leads to reduction in the calcium sparing effect, which can interfere with the normalization of serum calcium. Concomitant use of NATPARA with alendronate is not recommended.

Use in Specific Populations:

There are no adequate and well-controlled studies in pregnant women. Use during pregnancy only if the potential benefit justifies the potential risk to the fetus.

The safety and efficacy in pediatric patients have not been established

Please see [Full Prescribing Information](#), including Boxed Warning for potential risk of osteosarcoma.

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The companies in which Takeda directly and indirectly owns investments are separate entities. In this press release, “Takeda” is sometimes used for convenience where references are made to Takeda and its subsidiaries in general. Likewise, the words “we”, “us” and “our” are also used to refer to subsidiaries in general or to those who work for them. These expressions are also used where no useful purpose is served by identifying the particular company or companies.

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This press release and any materials distributed in connection with this press release may contain forward-looking statements, beliefs or opinions regarding Takeda’s future business, future position and results of operations, including estimates, forecasts, targets and plans for Takeda. Without limitation, forward looking statements often include the words such as “targets”, “plans”, “believes”, “hopes”, “continues”, “expects”, “aims”, “intends”, “ensures”, “will”, “may”, “should”, “would”, “could” “anticipates”, “estimates”, “projects” or words or terms of similar substance or the negative thereof. Any forward-looking statements in this document are based on the current assumptions and beliefs of Takeda in light of the information currently available to it. Such forward-looking statements do not represent any guarantee by Takeda or its management of future performance and involve known and unknown risks, uncertainties and other factors, including but not limited to: the economic circumstances surrounding Takeda’s business,

including general economic conditions in Japan, the United States and worldwide; competitive pressures and developments; applicable laws and regulations; the success of or failure of product development programs; decisions of regulatory authorities and the timing thereof; changes in exchange rates; claims or concerns regarding the safety or efficacy of marketed products or products candidates; and post-merger integration with acquired companies, any of which may cause Takeda's actual results, performance, achievements or financial position to be materially different from any future results, performance, achievements or financial position expressed or implied by such forward-looking statements. For more information on these and other factors which may affect Takeda's results, performance, achievements, or financial position, see "Item 3. Key Information—D. Risk Factors" in Takeda's Annual Report on Form 20-F filed with the U.S. Securities and Exchange Commission, available on Takeda's website at: <https://www.takeda.com/investors/reports/sec-filings/> or at www.sec.gov. Neither Takeda nor its management gives any assurances that the expectations expressed in these forward-looking statements will turn out to be correct, and actual results, performance or achievements could materially differ from expectations. Persons receiving this press release should not place undue reliance on forward looking statements. Takeda undertakes no obligation to update any of the forward-looking statements contained in this press release or any other forward-looking statements it may make, except as required by law or stock exchange rule. Past performance is not an indicator of future results and the results of Takeda in this press release may not be indicative of, and are not an estimate, forecast or projection of Takeda's future results.

About Takeda Pharmaceutical Company Limited

Takeda Pharmaceutical Company Limited ([TSE:4502/NYSE:TAK](https://www.tse-europe.com/quote/TSE:4502/NYSE:TAK)) is a global, values-based, R&D-driven biopharmaceutical leader headquartered in Japan, committed to bringing Better Health and a Brighter Future to patients by translating science into highly-innovative medicines. Takeda focuses its R&D efforts on four therapeutic areas: Oncology, Gastroenterology (GI), Rare Diseases and Neuroscience. We also make targeted R&D investments in Plasma-Derived Therapies and Vaccines. We are focusing on developing highly innovative medicines that contribute to making a difference in people's lives by advancing the frontier of new treatment options and leveraging our enhanced collaborative R&D engine and capabilities to create a robust, modality-diverse pipeline. Our employees are committed to improving quality of life for patients and to working with our partners in health care in approximately 80 countries and regions.

For more information, visit <https://www.takeda.com>.