COMPANY ANNOUNCEMENT

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

Summary

Company Announcement Date:

September 05, 2019

FDA Publish Date:

September 05, 2019

Product Type:

Drugs

Reason for Announcement:

Potential presence of rubber particulate

Company Name:

Takeda Pharmaceutical Company Limited

Brand Name:

Natpara

Product Description:

Parathyroid Hormone for Injection

Company Announcement

Takeda Pharmaceutical Company Limited (TSE:4502/NYSE:TAK (https://www.takeda.com/investors/) (http://www.fda.gov/about-fda/website-policies/website-disclaimer)) (“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.

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. (https://www.shirecontent.com/PI/PDFs/Natpara_USA_ENG.pdf) (http://www.fda.gov/about-fda/website-policies/website-disclaimer)

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 (/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program/reporting-serious-problems-fda)
- Regular Mail or Fax: Download form (/safety/medical-product-safety-information/forms-reporting-fda) or call 1- 800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178

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.

Limitationsof 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. (http://www.natpararems.com/) (http://www.fda.gov/about-fda/website-policies/website-disclaimer)

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.p 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, hypoaesthesia, 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.

Company Contact Information

Consumers:

Takeda Medical Information

+1-800-828-2088 and select Option 2

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