September 5, 2019

US Recall of NATPARA® (parathyroid hormone) for Injection

IMPORTANT INFORMATION REQUIRING ACTION

Dear Healthcare Provider,

The purpose of this letter is to inform you that Takeda has issued a US recall for all doses of NATPARA® (parathyroid hormone) for Injection (25 mcg, 50 mcg, 75 mcg, and 100 mcg). The recall is effective immediately. This recall is being conducted after discussions with the US Food and Drug Administration (FDA) and is 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 medicine solution. When the septum is repeatedly punctured, it is possible that small rubber fragments may detach into the cartridge.

The recall includes all doses of NATPARA. It is important that healthcare providers immediately contact their patients to help ensure safe discontinuation of NATPARA treatment.

The safety profile of NATPARA remains consistent with the product label.

In light of this recall, we would like to remind you that abrupt discontinuation of NATPARA or dose interruption in patients can result in severe hypocalcemia as stipulated in the NATPARA Full Prescribing Information:

> **2.6 NATPARA Dose Interruption or Discontinuation**
> Abrupt interruption or discontinuation of NATPARA can result in severe hypocalcemia. Resume treatment with, or increase the dose of, an active form of vitamin D and calcium supplements if indicated in patients interrupting or discontinuing NATPARA, monitor for signs and symptoms of hypocalcemia and serum calcium levels.
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> **5.4 Warnings and Precautions: Hypocalcemia**
> Severe hypocalcemia has been reported in patients taking NATPARA, including cases of hypocalcemia that resulted in seizures. The risk is highest when NATPARA is withheld, missed or abruptly discontinued, but can occur at any time. Monitor serum calcium and patients for signs and symptoms of hypocalcemia. Resume treatment with, or increase the dose of, an active form of vitamin D or calcium supplements or both if indicated in patients interrupting or discontinuing NATPARA to prevent severe hypocalcemia.

Therefore, as your patients discontinue NATPARA, it is very important to closely monitor serum calcium levels and observe for signs and symptoms of hypocalcemia in these patients while carefully titrating active vitamin D and supplemental calcium doses to maintain serum calcium levels within the lower half of the normal range (i.e., between 8 and 9 mg/dL). Please be aware that some patients may

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require doses of oral active vitamin D and supplemental calcium that are higher than that which they required prior to starting NATPARA.

As with any interruption in NATPARA treatment, you should notify your patients of the significant risk of severe hypocalcemia when discontinuing NATPARA and the need for close follow-up and the importance of urgently contacting you if they experience signs or symptoms of hypocalcemia.

Please know that your patients will be notified directly through Takeda OnePath® patient services and advised to contact you for your medical recommendations.

Takeda is committed to supply integrity, and we are working closely with the FDA to resolve the issue in a timely manner and resume supply.

Reporting Adverse Events
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

Medical Information
You may also contact our medical information department at 1-800-828-2088 if you have any questions about the information contained in this letter or the safe and effective use of NATPARA.

This letter is not intended as a complete description of the benefits and risks related to the use of NATPARA. Please refer to the enclosed full Prescribing Information and Medication Guide. For additional information, please call Takeda at 1-800-828-2088 or visit www.natpara.com.

Please see accompanying Full Prescribing Information, Medication Guide, and Instructions for Use for NATPARA attached.

Sincerely,

Tom Koutsavlis, MD, FRCPC
Head, US Medical

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Enclosure: NATPARA Full Prescribing Information

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