



March 23, 2022

Dear Healthcare Provider,

Takeda is providing a U.S. regulatory update for NATPARA® (parathyroid hormone) to inform you that the Company has received a Complete Response Letter (CRL) from the U.S. Food and Drug Administration (FDA) in response to the Prior Approval Supplement (PAS) submitted in August 2021. The NATPARA PAS proposed device component changes, including a new septum and new needle, to address the issue of rubber particulates originating from the rubber septum of the NATPARA cartridge that led to the US recall in September 2019. The CRL indicates that the FDA has completed its review of the NATPARA PAS and determined that it cannot be approved in its present form.

Takeda is evaluating the details of the CRL to determine next steps. In the meantime, we are deeply disappointed to inform the hypoparathyroidism community that NATPARA's commercial return in the U.S. is indefinitely delayed. Importantly, because there are no U.S. FDA-approved treatment alternatives for chronic hypoparathyroidism patients, Takeda intends to provide patients who are enrolled in the NATPARA Special Use Program (SUP) with continued access to therapy free of charge, in accordance with regulatory oversight and under the discretion of the FDA, until a commercial product is available.

With the goal of limiting supply interruption for SUP patients, we continue to work on the separate supply challenges surrounding protein particle formation that we have described over the past year. Those challenges are unrelated to the PAS and the recall. It is important to underscore that all product released for patient use continues to meet Takeda's quality standards and the safety profile of NATPARA has not changed.

We understand and have tremendous empathy for how much the community has been impacted without NATPARA and are disheartened to share this update. Takeda leaders will host a video teleconference with the US hypoparathyroidism community to provide more context regarding this communication in the coming weeks. Please watch for more information about that upcoming event in the NATPARA Updates section of our Takeda US Newsroom at <https://www.takeda.com/en-us/newsroom/natpara-updates/>. Information should be posted before the end of March. We will also share the information with the HypoPARAthyroidism Association and HypoPara Support & Advocacy.

Reporting Adverse Events

Healthcare providers and patients are encouraged to report adverse events in patients taking NATPARA to Takeda at 1-877-TAKEDA-7 (1-877-825-3327).

Adverse events, medication errors, or quality problems experienced with the use of this product may also be reported to the FDA's MedWatch Adverse Event Reporting Program either online, by regular mail, or by fax:

- Complete and submit the report Online: www.fda.gov/medwatch/report.htm
- Regular mail or Fax: Download form www.fda.gov/MedWatch/getforms.htm 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 (1-800-332-0178).

Medical Information

You may also contact our medical information department at 1-877-TAKEDA-7 (1-877-825-3327) 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 1-877-TAKEDA-7 (1-877-825-3327) or visit www.NATPARA.com.

Sincerely,

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

Tom Koutsavlis
Head, US Medical

Enclosures: NATPARA Full Prescribing Information

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US-NAT-0526v1.0 03/22