June 14, 2021

Dear Healthcare Provider,

The purpose of this letter is to notify you of **time-sensitive information that impacts your patient(s) receiving the 100-mcg dose of NATPARA® (parathyroid hormone) for Injection** through the NATPARA Special Use Program (SUP). As we have communicated previously, the extraordinary supply demands of the SUP have led to intermittent supply interruptions for patients receiving NATPARA 100-mcg through the SUP. Please see below for important information regarding a two-step approach to maintain supply continuity for these patients.

First, to prepare for a near-term anticipated supply interruption, we will activate the alternate prescriptions currently on file for SUP patients receiving NATPARA 100-mcg. These shipments will begin the week of June 21, 2021. If your patient does not have an alternate prescription on file, you have received a separate communication. If you have any questions regarding the SUP or the alternate prescription form on file, please contact your Takeda OnePath® Patient Support Manager at 1-866-888-0660, Monday through Friday 8:30AM – 8:00PM ET.

Second, to mitigate the potential for ongoing supply interruptions, a plan has been developed after consultation with the FDA. This new Adjusted 100-mcg Dosing Plan involves substituting a single injection of the 100-mcg dose with two consecutive injections of the 50-mcg dose from a single cartridge using the same needle. **In order to participate in this plan,** patients currently receiving NATPARA 100-mcg and their healthcare providers must both sign a new enrollment form specific to the SUP Adjusted 100-mcg Dosing Plan and return it within 14 days.

Special Use Program Adjusted 100-mcg Dosing Plan

For patients in the SUP, who in your independent clinical judgement are to continue at the 100-mcg daily dose, you may **substitute the 100-mcg injection with two (2) consecutive 50-mcg doses from the same cartridge**, which is an approach supported by pharmacokinetic data. Using each NATPARA cartridge for only one needle puncture of the cartridge septum substantially decreases the risk for formation of rubber particles because this risk increases when the septum is repeatedly punctured as may occur during once daily 14-day use. The two (2) doses should be given from one cartridge *within 15 minutes* as follows:

1. The patient (or caregiver) cleans the surface where the pen device will be placed.
2. The patient (or caregiver) follows the NATPARA Instructions for Use (IFU) to reconstitute a 50-mcg cartridge and delivers the first injection of 50-mcg.
3. The patient (or caregiver) takes the needle out of the skin, but does not remove the needle from the device, and carefully puts the pen flat down on a clean surface.
4. The patient (or caregiver) chooses a new injection site on the alternate thigh, cleans the site with an alcohol pad and lets it dry.
5. The patient (or caregiver) turns the dosage knob for a second 50-mcg dose and performs another injection at the new site within 15 minutes of the first injection.
6. The patient (or caregiver) removes the needle from the skin and discards the needle per the IFU.
7. The patient (or caregiver) checks the cartridge dose indicator to confirm 2 doses of 50-mcg has been delivered from the cartridge.

Using the same needle to deliver 2 doses from one cartridge ensures that the cartridge is punctured only once.

Due to ongoing supply constraints, the Adjusted 100-mcg Dosing Plan will be the only sustainable 100-mcg daily equivalent regimen available, and failure to provide 100-mcg patients with an updated prescription will result in patient supply disruption.

ACTION REQUIRED

A new prescription will be required in order to fulfill and ship your patient the new dosing option (two consecutive doses of NATPARA 50-mcg in place of one dose of NATPARA 100-mcg) as well as to support nurse training. If you have a patient that is currently receiving 100-mcg and agree to this treatment option, it is important that you **submit the updated enrollment form** (NATPARA Special Use Program Adjusted 100-mcg Dosing Plan Enrollment Form) **to avoid a disruption in your patient's NATPARA treatment.** Please fax the completed enrollment form to **844-284-3234** within 14 days of receipt of this letter. Both you and your patient will need to sign the enrollment form, indicating agreement to adhere to the updated SUP Terms and Conditions. Upon receipt of the completed enrollment form, OnePath® will coordinate delivery and schedule nurse training for your patient.

Please also note that in order to account for the use of two (2) doses per cartridge, the SUP Terms and Conditions will be updated such that the expectation will be a return of the NATPARA product after one (1) use for any remaining supply of NATPARA 100-mcg and after two (2) doses per day once the patient transitions to 50-mcg cartridges, providing that the patient's total prescribed daily dose is 100-mcg.

It is important to discuss these changes with your patient and to educate your patient and/or caregiver on the new dosing method with an in-person or virtual visit. Please also emphasize to your patient(s) (caregivers) the importance of cleaning the injection sites with alcohol pads and remembering to perform the second injection within 15 minutes at the new injection site on the alternate thigh. A member of Takeda's OnePath Patient Services team will also reach out to your patient to ensure information has been received, offer support, and arrange for product administration training.

For any of your patients who may be affected by a NATPARA dose interruption, please review Section 2.6 (NATPARA Dose Interruption or Discontinuation) and Section 5.4 (Warnings and Precautions: Hypocalcemia) in the attached NATPARA Full Prescribing Information. It is very important to closely monitor serum calcium levels and observe for signs and symptoms of hypocalcemia in these patients while carefully adjusting active vitamin D and supplemental calcium doses. Some patients may require higher doses of active vitamin D and supplemental calcium than doses required prior to starting NATPARA. Additional guidance regarding NATPARA treatment interruption was previously issued in a joint statement by the Endocrine Society and American Society for Bone and Mineral Research (ASBMR) at the following URL: https://endocrinenews.endocrine.org/endocrine-society-asbmr-issue-joint-statement-on-natpara-recall/.

Reporting Adverse Events

Healthcare providers and patients are encouraged to report adverse events in patients taking NATPARA to Takeda at 1-800-828-2088.

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,

Tom Koutsavlis
Head, US Medical

Enclosures: NATPARA Full Prescribing Information
Patient/Caregiver Injection Instructions For Adjusted 100-mcg Dosing Plan
NATPARA Special Use Program Adjusted 100-mcg Dosing Plan Enrollment Form

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