

**Initial REMS Approval: 01/2015**

**Modified REMS: 09/2016**

**BLA 125511**

**NATPARA<sup>®</sup> (parathyroid hormone) for injection**

**Recombinant human parathyroid hormone (1-84)**

Shire

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## **RISK EVALUATION AND MITIGATION STRATEGY (REMS)**

### **I. GOAL**

The goal of the NATPARA REMS Program is to mitigate the potential risk of osteosarcoma associated with NATPARA by:

- a. ensuring that prescribers are educated on the following:
  - potential risk of osteosarcoma associated with the use of NATPARA
  - appropriate patient selection
  - safe-use conditions required for prescribing NATPARA
- b. ensuring that NATPARA is dispensed only to patients informed about the potential risk of osteosarcoma associated with the use of NATPARA

## II. REMS Elements

### A. Elements to Assure Safe Use (ETASU)

#### 1. Healthcare providers who prescribe NATPARA are specially certified.

- a. To become specially certified to prescribe NATPARA in the NATPARA REMS Program, healthcare providers must:
  - i. Review the Prescribing Information for NATPARA.
  - ii. Review the *NATPARA REMS Program: An Introduction*.
  - iii. Review and successfully complete the *NATPARA REMS Program Training Module for Prescribers* including the *Knowledge Assessment*.
  - iv. Enroll in the NATPARA REMS Program by completing the *NATPARA REMS Program Prescriber Enrollment Form*
  - v. Agree on the *NATPARA REMS Program Prescriber Enrollment Form* to:
    - 1) Review the *NATPARA REMS Program Patient Brochure* with each patient to inform patients about the appropriate use and risks associated with NATPARA, and provide the patient a copy.
    - 2) Complete and sign the *NATPARA REMS Program Patient-Prescriber Acknowledgment Form* for each patient receiving a prescription for NATPARA. The prescriber must send a copy of the signed *NATPARA REMS Program Patient-Prescriber Acknowledgment Form* to the NATPARA REMS Program Coordinating Center by fax at 1-844-NAT-REMS (628-7367) or scan and email to NATPARAREMS@shire.com and store a copy of the form in the patient's record.
- b. Shire must:
  - i. Ensure that healthcare providers who prescribe NATPARA are specially certified, in accordance with the requirements described above.
  - ii. Provide all the following mechanisms for healthcare providers to complete the certification process for NATPARA REMS Program: online, fax, email.

- iii. Ensure that healthcare providers are notified when they have been certified by the NATPARA REMS Program.
- iv. Maintain a validated, secure database of healthcare providers who are certified to prescribe NATPARA in the NATPARA REMS Program.
- v. Ensure that healthcare providers meet the REMS certification requirements and de-certify healthcare providers who do not maintain compliance with prescriber certification requirements.
- vi. Provide the *NATPARA REMS Program: An Introduction* information sheet, *NATPARA REMS Program Training Module for Prescribers*, *NATPARA REMS Program Prescriber Enrollment Form*, *NATPARA REMS Program Patient Brochure*, *NATPARA REMS Program Patient-Prescriber Acknowledgment Form*, and the Prescribing Information to healthcare providers who (1) attempt to prescribe NATPARA and are not yet certified, or (2) inquire about how to become certified.
- vii. Ensure that REMS materials are available on the NATPARA REMS Program website ([www.NATPARAREMS.com](http://www.NATPARAREMS.com)) or by calling the NATPARA REMS Program Coordinating Center at 1-855-NATPARA (628-7272).

The following materials are part of the NATPARA REMS Program and are appended:

- *NATPARA REMS Program: An Introduction*
- *NATPARA REMS Program Training Module for Prescribers*
- *NATPARA REMS Program Prescriber Enrollment Form*
- *NATPARA REMS Program Patient Brochure*
- *NATPARA REMS Program Patient-Prescriber Acknowledgment Form*

## **2. Pharmacies that dispense NATPARA are specially certified.**

- a. To become specially certified to dispense NATPARA in the NATPARA REMS Program, pharmacies must:
  - i. Designate an authorized representative to complete the certification process on behalf of the pharmacy.

- ii. Ensure the authorized representative must oversee implementation and compliance with the NATPARA REMS Program requirements by:
  - 1) Reviewing the Prescribing Information for NATPARA.
  - 2) Reviewing the *NATPARA REMS Program: An Introduction*.
  - 3) Reviewing and successfully completing the *NATPARA REMS Program Training Module for Pharmacy Representatives*, including the *Knowledge Assessment*.
  - 4) Completing the *NATPARA REMS Program Pharmacy Enrollment Form*.
  - 5) Ensuring that all relevant staff involved in the dispensing of NATPARA are trained on the NATPARA REMS Program requirements as described in the *NATPARA REMS Program Training Module for Pharmacy Representatives*.
  - 6) Putting processes and procedures in place, and following such processes and procedures, to ensure the following requirements are completed prior to dispensing NATPARA:
    - a) Verifying that the prescriber is certified in the NATPARA REMS Program by reviewing the prescriber's information against a list of REMs certified prescribers sent from the NATPARA REMS Program Coordinating Center.
    - b) Verifying that a *NATPARA REMS Program Patient-Prescriber Acknowledgment Form* has been completed and submitted by verifying that the patient and the prescriber are included in a list of REMS-approved patients and prescribers available through the NATPARA REMS Program Coordinating Center.
- iii. Agree to be audited by Shire, FDA, or a third party to ensure that all training, processes and procedures are in place and are being followed for the NATPARA REMS Program and appropriate documentation is maintained and available upon request.
- iv. Provide prescription data to the NATPARA REMS Program.

- v. Refrain from reselling or transferring NATPARA to other pharmacies or distributors.
  - vi. Recertify in the NATPARA REMS Program if the pharmacy designates someone else as the authorized representative.
- b. A Pharmacy must dispense NATAPRA to a patient only after verifying a *NATPARA REMS Program Patient-Prescriber Acknowledgment Form* is on record and the prescribing healthcare provider is certified in the NATPARA REMS Program.
- c. Shire must:
- i. Ensure that NATPARA is dispensed only by pharmacies that are specially certified.
  - ii. Provide all the following mechanisms for pharmacies to complete the certification process for the NATPARA REMS Program: fax or email.
  - iii. Ensure that the authorized representative is notified when the pharmacy has been certified by the NATPARA REMS Program.
  - iv. Ensure that certified pharmacies are provided a list daily of certified prescribers and records documenting receipt of *NATPARA REMS Program Patient-Prescriber Acknowledgment Forms*.
  - v. Verify every 2 years that the authorized representative's name and contact information corresponds to that of the current designated authorized representative for the certified pharmacy. If different, the pharmacy must be required to re-certify with a new appointed authorized representative.
  - vi. Provide the *NATPARA REMS Program: An Introduction*, *NATPARA REMS Program Training Module for Pharmacy Representatives*, *NATPARA REMS Program Pharmacy Enrollment Form*, and the Prescribing Information to pharmacies that inquire about how to become certified.

The following materials are part of the NATPARA REMS Program and are appended:

- *NATPARA REMS Program Training Module for Pharmacy Representatives*
- *NATPARA REMS Program Pharmacy Enrollment Form*

**3. NATPARA must be dispensed to patients with evidence or other documentation of safe-use conditions.**

- a. NATPARA must be dispensed only to patients who have been counseled about the potential risk of osteosarcoma and completed and signed a *NATPARA REMS Program Patient-Prescriber Acknowledgment Form*.
- b. Shire must:
  - i. Ensure that the certified prescriber is able to submit the completed *NATPARA REMS Program Patient-Prescriber Acknowledgment Form* to the NATPARA REMS Program Coordinating Center by fax at 1-844-NAT-REMS (628-7367), or scan and email to NATPARAREMS@shire.com.
  - ii. Ensure that the certified pharmacy is able to verify prior to dispensing that each patient prescribed NATPARA has completed and signed a *NATPARA REMS Program Patient-Prescriber Acknowledgment Form*.

**B. Implementation System**

1. Shire must ensure that NATPARA is distributed to and dispensed only by certified pharmacies by:
  - a. Ensuring that wholesalers/distributors who distribute NATPARA to certified pharmacies comply with the program requirements for wholesalers/distributors. In order for a wholesalers/distributor to distribute NATPARA, the wholesalers/distributor must:
    - i. Put processes and procedures in place to verify, prior to distributing NATPARA, that the pharmacies are certified.
    - ii. Train all relevant staff on the NATPARA REMS Program requirements.

- iii. Agree to be audited by Shire, FDA, or a third party to ensure that all processes and procedures are in place and are being followed for the NATPARA REMS Program and appropriate documentation is maintained and available upon request.
    - iv. Provide distribution data to the NATPARA REMS Program.
  2. Ensuring that wholesalers/distributors maintain distribution records of all shipments of NATPARA to certified pharmacies and provide the data to the NATPARA REMS Program Coordinating Center. Shire must send the distributors/wholesalers a list of certified pharmacies every month or anytime there is a new certified pharmacy added.
  3. Shire must monitor distribution data and audit the wholesalers/distributors within 180 days after the first shipment of NATPARA by wholesaler/distributor to ensure that all processes and procedures are in place and functioning to support the requirements of the NATPARA REMS Program. Corrective action must be instituted by Shire if noncompliance is identified.
  4. Shire must send confirmation of certification to each certified pharmacy.
  5. Shire must monitor and audit certified pharmacies within 30 days after the pharmacy is certified to ensure that all processes and procedures are in place and functioning to support the requirements of the NATPARA REMS Program. Corrective action must be instituted by Shire if noncompliance is identified. The certified pharmacy must also be included in Shire ongoing annual audit plan.
  6. Shire must maintain a validated, secure database of pharmacies that are certified to dispense NATPARA in the NATPARA REMS Program.
  7. Shire must maintain adequate records of NATPARA distribution/dispensing, certified prescribers, pharmacies, health care settings, distributors/wholesalers, and patients, to meet REMS requirements.

8. Shire must ensure that the REMS requirements are met and de-certify pharmacies that do not maintain compliance with pharmacy certification requirements.
9. Shire must maintain a NATPARA REMS Program Coordinating Center (1-855-NATPARA (628-7272)) with a call center to support patients, prescribers, and pharmacies in interfacing with the NATPARA REMS Program.
10. Shire must maintain a NATPARA REMS Program Website ([www.NATPARAREMS.com](http://www.NATPARAREMS.com)). The NATPARA REMS Program Website must include the capability to complete prescriber certification online. The NATPARA REMS Program Website must include the option to print the prescribing information, Medication Guide, and NATPARA REMS Program materials. The NATPARA product website must include a prominent REMS-specific link to NATPARA REMS Program Website.
11. Shire must ensure that within 60 calendar days of the approval of the REMS modification that the NATPARA REMS Program Website is fully operational and the REMS materials listed in or appended to the NATPARA REMS Document are available through the NATPARA REMS Program Website or by calling the NATPARA REMS Program Coordinating Center.
12. Shire must take reasonable steps to improve implementation of and compliance with the requirements in the NATPARA REMS Program based on monitoring and evaluation of the NATPARA REMS Program.

### **C. Timetable for Submission of Assessments**

Shire must submit REMS Assessments to FDA at 6 months, 12 months, and annually thereafter from the date of initial approval of the NATPARA REMS. To facilitate inclusion of as much information as possible, while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment

should conclude no earlier than 60 days before the submission date for that assessment. Shire must submit each assessment so that it will be received by FDA on or before the due date.