BLA 125511

NATPARA® (parathyroid hormone) for injection
Recombinant human parathyroid hormone (1-84)

NPS Pharmaceuticals
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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 Training Module for Prescribers including the Knowledge Assessment section.
      iv. Enroll in the NATPARA REMS Program by completing, signing and sending the NATPARA REMS Prescriber Enrollment Form to the NATPARA REMS Program Coordinating Center by fax at 844-NAT-REMS (628-7367) or email at NATPARAREMS@NPSP.COM.
      v. Agree on the NATPARA REMS Prescriber Enrollment Form to:
         1) Review the NATPARA 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 Patient-Prescriber Acknowledgment Form for each patient receiving a prescription for NATPARA. The prescriber will send a copy of the signed NATPARA REMS Patient-Prescriber Acknowledgment Form to the NATPARA REMS Program Coordinating Center by fax at 844-NAT-REMS (628-7367) or email at NATPARAREMS@NPSP.COM and will store a copy of the form in the patient's record.
   b. NPS Pharmaceuticals will:
      i. Ensure that healthcare providers who prescribe NATPARA are specially certified, in accordance with the requirements described above.
      ii. Ensure that prescriber certification process can be completed by sending the Knowledge Assessment and enrollment to the NATPARA REMS Program Coordinating Center via fax 844-NAT-REMS (628-
iii. Ensure that prescribers are notified when they have been certified by the NATPARA REMS Program.

iv. Maintain a validated, secure database of prescribers who are certified to prescribe NATPARA in the NATPARA REMS Program.

v. Ensure that prescribers meet the REMS certification requirements and may de-certify prescribers who do not maintain compliance with prescriber certification requirements.

vi. Provide the NATPARA REMS Program: An Introduction information sheet, NATPARA REMS Training Module for Prescribers, NATPARA REMS Prescriber Enrollment Form, NATPARA Patient Brochure, NATPARA REMS Patient-Prescriber Acknowledgment Form, and the Prescribing Information to prescribers 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 Website (www.NATPARAREMS.com) or by calling the NATPARA REMS Coordinating Center at (855) 628-7272.

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

- NATPARA REMS Program: An Introduction
- NATPARA REMS Training Module for Prescribers
- NATPARA REMS Prescriber Enrollment Form
- NATPARA Patient Brochure
- NATPARA REMS 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 will 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 Training Module for Pharmacy Representatives, including the Knowledge Assessment section.
   4) Completing the REMS Pharmacy Enrollment Form and submitting to the NATPARA REMS Coordinating Center by fax at 844-NATREMS (628-7367) or email at NATPARAREMS@NPSP.COM.
   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 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 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 NPS Pharmaceuticals, 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 Patient-Prescriber Acknowledgment Form* is on record
and the prescribing healthcare provider is certified in the NATPARA
REMS Program.

c. NPS Pharmaceuticals will:

i. Ensure that NATPARA is dispensed only by pharmacies that are
specially certified.

ii. Ensure that pharmacy certification process can be completed by
sending the *Knowledge Assessment* and enrollment to the NATPARA
REMS Program Coordinating Center via fax (844-628-7367) or email at
NATPARAREMS@NPSP.COM.

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
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 will be required to re-certify with a new appointed
authorized representative.

vi. Provide the *NATPARA REMS Program: An Introduction, NATPARA
REMS Training Module for Pharmacy Representatives, NATPARA*
REMS 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 Training Module for Pharmacy Representatives
- NATPARA REMS Pharmacy Enrollment Form

3. NATPARA will be dispensed to patients with evidence or other documentation of safe-use conditions.
   a. NATPARA will be dispensed only to patients who have been counseled about the potential risk of osteosarcoma and completed and signed a NATPARA REMS Patient-Prescriber Acknowledgment Form.
   b. NPS Pharmaceuticals will:
      i. Ensure that the certified prescriber is able to submit the completed NATPARA REMS Patient-Prescriber Acknowledgment Form to the NATPARA REMS Program Coordinating Center by fax at 844-NATREMS (628-7367) or by email at NATPARAREMS@NPSP.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 Patient-Prescriber Acknowledgment Form.

B. Implementation System

1. NPS Pharmaceuticals will 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 NPS Pharmaceuticals, 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. NPS Pharmaceuticals will send the distributors/wholesalers a list of certified pharmacies every month or anytime there is a new certified pharmacy added.

3. NPS Pharmaceuticals will 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 will be instituted by NPS Pharmaceuticals if noncompliance is identified.

4. NPS Pharmaceuticals will send confirmation of certification to each certified pharmacy.

5. NPS Pharmaceuticals will 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 will be instituted by NPS Pharmaceuticals if noncompliance is identified. The certified pharmacy will also be included in NPS Pharmaceuticals’ ongoing annual audit plan.
6. NPS Pharmaceuticals will maintain a validated, secure database of pharmacies that are certified to dispense NATPARA in the NATPARA REMS Program.

7. NPS Pharmaceuticals will maintain adequate records of NATPARA distribution/dispensing, certified prescribers, pharmacies, healthcare settings, distributors/wholesalers, and patients, to meet REMS requirements.

8. NPS Pharmaceuticals will ensure that the REMS requirements are met and may de-certify pharmacies that do not maintain compliance with pharmacy certification requirements.

9. NPS Pharmaceuticals will maintain a NATPARA REMS Program Coordinating Center with a call center to support patients, prescribers, and pharmacies in interfacing with the NATPARA REMS Program.

   iii. NPS Pharmaceuticals will ensure that all materials listed in or appended to the NATPARA REMS Program are available through the NATPARA REMS Website at www.NATPARAREMS.com or from the NATPARA REMS Program Coordinating Center at (855) 628-7272.

10. NPS Pharmaceuticals will 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.

11. NPS REMS website for healthcare professionals (www.NATPARAREMS.com) will continue for the duration of the REMS. The NATPARA REMS website will include the option to print versions of the NATPARA REMS materials. The NATPARA website for healthcare professionals will include a prominent REMS-specific link to NATPARA REMS website.

C. Timetable for Submission of Assessments
NPS Pharmaceuticals will 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. NPS Pharmaceuticals will submit each assessment so that it will be received by FDA on or before the due date.