February 5, 2021

Dear Valued Patient,

We're sending you this letter because you are prescribed NATPARA (parathyroid hormone) 75-mcg or NATPARA 100-mcg through the Special Use Program and your OnePath® Patient Support Manager has been unable to reach you by phone.

We are providing you with this letter to inform you of a potential shipping delay. An inventory processing delay, compounded by a severe winter storm during the week of February 1, 2021, has impacted the NATPARA® shipping schedule. There are some patients who could experience a brief supply interruption of NATPARA 75-mcg or NATPARA 100-mcg between now and the end of the second week of February. It is therefore with a sense of urgency that we are contacting you at this time. Pending any additional unanticipated delays, we have already rescheduled shipments and expect the supply interruption to be fully addressed by February 11, 2021.

ACTION NEEDED: Please contact your OnePath Patient Support Manager at 866-888-0660 at your earliest convenience so we can provide you with urgent information related to your NATPARA shipments and your prescribing physician.

We are in the process of communicating with all prescribing physicians to notify them about this inventory issue and shipping delay. If a new prescription is needed, based on your physician's medical judgement, please make sure your prescribing physician contacts Takeda OnePath at 866-888-0660 as soon as possible. If your Physician has previously submitted an alternative back-up prescription form, that alternative prescription will be filled to avoid an interruption. Our goal is to supply you with the backup prescription that is on file, if needed. Your regular prescription will resume once that dose is again available. A Takeda OnePath® Patient Support Manager will follow up with you and answer questions related to the processing of this prescription or your scheduled shipments.

This shipping delay is NOT the result of any quality or manufacturing issues. This situation is not impacting NATPARA 50-mcg or NATPARA 25-mcg. However, based on the supply demands of the Special Use Program, we continue to closely monitor all NATPARA doses. We are committed to supply continuity and will provide a general update on all NATPARA doses by the end of March 2021.

As a patient who is receiving NATPARA through the Special Use Program, we want to remind you that each NATPARA cartridge under the Special Use Program (single dose use) is intended for one use only, and that used cartridges with remaining product are to be returned to Takeda in accordance with the Special Use Program (single dose use) instructions. Non-compliance with the rules under the Special Use Program (single dose use) could result in termination of your ability to receive NATPARA product through the program.

It is important to remember that any potential interruption or reduction in the daily dose of NATPARA can cause a decrease in blood calcium levels (severe hypocalcemia) which can be dangerous. We appreciate your patience.

We recognize the important medical need that NATPARA fills for patients like you who are living with chronic hypoparathyroidism. We appreciate your patience.

Cheryl Schwartz — Head of U.S. Rare Disease Business Unit

Rick Ascroft — Senior Vice President, Patient Services & Managed Markets

What is NATPARA® (parathyroid hormone) for Injection?

- NATPARA is a prescription parathyroid hormone used with calcium and vitamin D to control low blood calcium (hypocalcemia) in people with low parathyroid hormone blood levels (hypoparathyroidism).
- NATPARA is only for people who do not respond well to treatment with calcium and active forms of vitamin D alone, because it may increase the possible risk of bone cancer (osteosarcoma).
- NATPARA was not studied in people with hypoparathyroidism caused by calcium-sensing receptor mutations.
- NATPARA was not studied in people who get sudden hypoparathyroidism after surgery.
- It is not known if NATPARA is safe and effective for children 18 years of age and younger. NATPARA should not be used in children and young adults whose bones are still growing.

Important Safety Information
What is the most important information I should know about NATPARA?
Warning: Possible bone cancer (osteosarcoma).

- During animal drug testing, NATPARA caused some rats to develop a bone cancer called osteosarcoma. It is not known if people who take NATPARA will have a higher chance of getting osteosarcoma. Tell your doctor right away if you have pain in any areas of your body that does not go away, or any new or unusual lumps or swelling under your skin that is tender to touch.

- **NATPARA is only available through the NATPARA Risk Evaluation and Mitigation Strategy (REMS) Program.** The purpose of the NATPARA REMS program is to inform patients about the potential risk of osteosarcoma associated with the use of NATPARA. For more information about this REMS program, call 1-855-NATPARA (628-7272) or go to www.NATPARAREMS.com.

NATPARA may cause other serious side effects, including:

High blood calcium (hypercalcemia)

- NATPARA can cause some people to have a higher blood calcium level than normal.

1. Your doctor should check your blood calcium before you start and during your treatment with NATPARA.
2. Tell your doctor if you have nausea, vomiting, constipation, low energy, or muscle weakness. These may be signs that you have too much calcium in your blood.

Low blood calcium (hypocalcemia)

- People who stop using or miss a dose of NATPARA may have an increased risk of severe low blood calcium levels.
- Tell your doctor if you have tingling of your lips, tongue, fingers and feet, twitching of face muscles, cramping of feet and hands, seizures, depression, or have problems thinking or remembering.

Who should not use NATPARA?

- **Do not use NATPARA** if you are allergic to parathyroid hormone or any of the ingredients in NATPARA.

What should I tell my healthcare provider before using NATPARA?

- **Before you start using NATPARA, tell your doctor about all of your medical conditions. Tell your doctor about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

What are the possible side effects of NATPARA?

- **NATPARA may cause serious side effects like allergic (hypersensitivity) reaction, including anaphylaxis**. Tell your healthcare provider or get emergency medical help right away if you have any of the following symptoms of an allergic reaction:
  - swelling of your face, lips, mouth, or tongue
  - breathing problems
  - fainting, dizziness, feeling lightheaded (low blood pressure)
  - fast heartbeat
  - itching
  - rash
  - hives

- **The most common side effects of NATPARA include:** tingling, tickling, or burning feeling of the skin, low or high blood calcium, headache, nausea, reduced sense of touch or sensation, diarrhea, vomiting, pain in joints, too much calcium in urine, and pain in limbs.

Enclosure: NATPARA Full Prescribing Information

US-NAT-0369v1.0 2/21

December 22, 2020

Dear Valued Patient,

We are writing to share a supply-status update to the information we provided during the week of December 14, regarding the potential for near-term supply interruptions of NATPARA® (parathyroid hormone) for Injection that may impact U.S. patients receiving NATPARA through the Special Use Program.

Since that supply update, the manufacturing disruption impacting the availability of NATPARA 100-mcg and NATPARA 75-mcg has now been mitigated. **This means that we are no longer expecting near-term supply interruptions for any NATPARA dose for patients receiving NATPARA through the Special Use Program**. You will continue to receive NATPARA through the Special Use Program according to your current shipping schedule.

Your Takeda OnePath® Patient Support Manager will contact you in the coming days to provide the update that we are no longer expecting near-term supply interruptions for NATPARA and to answer questions related to your next NATPARA shipment or the Special Use Program. If you have any immediate questions or concerns, please contact your Takeda OnePath® Patient Support Manager at 866-888-0660. Patient Support Managers are available Monday through Friday 8:30 AM – 8:00 PM ET.

At this time, we do not anticipate near-term supply interruptions for any NATPARA dose. However, we are closely monitoring all NATPARA doses based on the supply demands of the Special Use Program. We are committed to supply continuity and will provide another update on all NATPARA doses by March 2021.

As a patient who is receiving NATPARA through the Special Use Program, we want to remind you that each NATPARA cartridge under the Special Use Program (single dose use) is intended for one use only, and that used cartridges with remaining product are to be returned to Takeda in accordance with the Special Use Program (single dose use) instructions. Non-compliance with the rules under the Special Use Program (single dose use) could result in termination of your ability to receive NATPARA product through the program.

Enclosed for your reference is the full NATPARA Prescribing Information and Medication Guide. For additional medical information, please contact your healthcare provider.

We recognize that we have been communicating about supply frequently since October 2020, and we are doing that to ensure that you and your prescriber have time to discuss treatment plans in the event of actual NATPARA supply interruptions. This is especially important because any potential interruption or reduction in the daily dose of NATPARA can cause a sharp

decrease in blood calcium levels (severe hypocalcemia) which can be dangerous. We appreciate your patience during the past few months as we worked to maintain supply continuity.

Wishing you and your family a happy and healthy holiday season,

Cheryl Schwartz
Head of U.S. Rare Disease Business Unit

Daniel McNamara
Head of U.S. Patient Services

What is NATPARA® (parathyroid hormone) for Injection?

- NATPARA is a prescription parathyroid hormone used with calcium and vitamin D to control low blood calcium (hypocalcemia) in people with low parathyroid hormone blood levels (hypoparathyroidism).
- NATPARA is only for people who do not respond well to treatment with calcium and active forms of vitamin D alone, because it may increase the possible risk of bone cancer (osteosarcoma).
- NATPARA was not studied in people with hypoparathyroidism caused by calcium-sensing receptor mutations.
- NATPARA was not studied in people who get sudden hypoparathyroidism after surgery.
- It is not known if NATPARA is safe and effective for children 18 years of age and younger. NATPARA should not be used in children and young adults whose bones are still growing.

Important Safety Information
What is the most important information I should know about NATPARA?
Warning: Possible bone cancer (osteosarcoma).

- During animal drug testing, NATPARA caused some rats to develop a bone cancer called osteosarcoma. It is not known if people who take NATPARA will have a higher chance of getting osteosarcoma. Tell your doctor right away if you have pain in any areas of your body that does not go away, or any new or unusual lumps or swelling under your skin that is tender to touch.

- **NATPARA is only available through the NATPARA Risk Evaluation and Mitigation Strategy (REMS) Program.** The purpose of the NATPARA REMS program is to inform patients about the potential risk of osteosarcoma associated with the use of NATPARA. For more information about this REMS program, call 1-855-NATPARA (628-7272) or go to www.NATPARAREMS.com.

NATPARA may cause other serious side effects, including:

High blood calcium (hypercalcemia)

- NATPARA can cause some people to have a higher blood calcium level than normal.

1. Your doctor should check your blood calcium before you start and during your treatment with NATPARA.

Low blood calcium (hypocalcemia)

- People who stop using or miss a dose of NATPARA may have an increased risk of severe low blood calcium levels.
- Tell your doctor if you have tingling of your lips, tongue, fingers and feet, twitching of face

2. Tell your doctor if you have nausea, vomiting, constipation, low energy, or muscle weakness. These may be signs that you have too much calcium in your blood.

muscles, cramping of feet and hands, seizures, depression, or have problems thinking or remembering.

Who should not use NATPARA?

- **Do not use NATPARA** if you are allergic to parathyroid hormone or any of the ingredients in NATPARA.

What should I tell my healthcare provider before using NATPARA?

- **Before you start using NATPARA, tell your doctor about all of your medical conditions. Tell your doctor about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

What are the possible side effects of NATPARA?

- **NATPARA may cause serious side effects like allergic (hypersensitivity) reaction, including anaphylaxis**. Tell your healthcare provider or get emergency medical help right away if you have any of the following symptoms of an allergic reaction:
  - swelling of your face, lips, mouth, or tongue
  - breathing problems
  - fainting, dizziness, feeling lightheaded (low blood pressure)
  - fast heartbeat
  - itching
  - rash
  - hives

- **The most common side effects of NATPARA include:** tingling, tickling, or burning feeling of the skin, low or high blood calcium, headache, nausea, reduced sense of touch or sensation, diarrhea, vomiting, pain in joints, too much calcium in urine, and pain in limbs.

Enclosure: NATPARA Full Prescribing Information

December 16th, 2020

Dear Valued Patient,

We are writing to provide the latest update regarding the potential for near-term supply interruptions of multiple doses of NATPARA® (parathyroid hormone) for Injection that may impact U.S. patients receiving NATPARA through the Special Use Program (SUP). While we work with urgency to avoid any supply interruptions for patients receiving NATPARA through the SUP, our priority is to ensure that you and your prescriber are prepared in the event of an actual supply interruption. Given the fluid nature of the situation, we could have additional information available as soon as the week of December 21, 2020.

If you are receiving NATPARA 100-mcg or NATPARA 75-mcg, please see the following time-sensitive information regarding the immediate actions you must take. If you are receiving other doses of NATPARA, there's nothing you need to do at this time. However, supply status updates for all other NATPARA doses are also included in this letter.

IMMEDIATE ACTION REQUIRED FOR PATIENTS RECEIVING NATPARA 75-MCG OR NATPARA 100-MCG

If you have not yet contacted your prescribing physician to determine the best treatment plan for you, please contact him/her as soon as possible. Since our update during the week of November 16, we are now preparing for a potential near-term supply interruption of **NATPARA 75-mcg**, in addition to the anticipated supply interruption of **NATPARA 100-mcg**. Based on our current assessments, we are anticipating supply interruptions for NATPARA 100-mcg as early **as January 2, 2021**, as well as for NATPARA 75-mcg, as early as **mid-January.**

Based on your prescriber's independent medical judgement, your revised treatment plan may require a new prescription. Please ensure you work closely with your prescribing physician on any changes to your treatment plan, including the potential for a new prescription.

****Please note that if you are currently receiving NATPARA 100-mcg or NATPARA 75-mcg and you have not received an updated prescription, or if your prescriber has provided a modified dose for NATPARA 100-mcg that includes the 75-mcg dose of NATPARA, please contact your physician as soon as possible. For patients receiving NATPARA 100-mcg, we would need to receive an updated prescription form from your physician by December 22, 2020 and if you are a patient receiving NATPARA 75-mcg, we would need to receive an updated prescription form by January 8, 2021 in order to continue to ship medication to you. Updated prescription forms not received by these dates will result in disruption in shipments to you.**

However, if your physician has already submitted an updated prescription form in anticipation of a potential supply interruption, and that updated prescription does not include the 75-mcg dose of NATPARA, there's nothing more you need to do. Your Takeda OnePath® Patient Support Manager will provide you with the shipment timing information for your updated prescription.

Patient safety is Takeda's main priority and, as a patient enrolled in the Special Use Program who is receiving **NATPARA 75-mcg** or **NATPARA 100-mcg**, we are alerting you and your prescribing physician

that any potential interruption or reduction in the daily dose of NATPARA can cause a sharp decrease in blood calcium levels (severe hypocalcemia) which can be dangerous. It is important for you to work closely with your healthcare provider for important medical recommendations, including frequent monitoring of your blood calcium levels and close titration of active vitamin D and calcium supplements if you stop or alter your dose as a result of this supply interruption to avoid hypocalcemia.

Update Regarding NATPARA 25-mcg and 50-mcg:

At this time, we do **not** expect SUP-enrolled patients who are receiving **NATPARA 25-mcg or NATPARA 50-mcg** to be impacted by near-term supply interruptions. However, we are closely monitoring all NATPARA doses based on the supply demands of the Special Use Program. We are committed to supply continuity and will provide another update on all NATPARA doses by mid-January. We have also communicated to physicians who have prescribed NATPARA 25-mcg or NATPARA 50-mcg that there is nothing they need to do at this time.

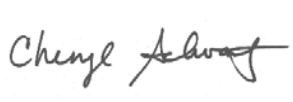
As a patient who is receiving NATPARA through the Special Use Program, we want to remind you that each NATPARA cartridge under the Special Use Program (single dose use) is intended for one use only, and that used cartridges with remaining product are to be returned to Takeda in accordance with the Special Use Program (single dose use) instructions. Non-compliance with the rules under the Special Use Program (single dose use) could result in termination of your ability to receive NATPARA product through the program.

OnePath will continue to work closely with your prescribing physician to support your treatment plan. If you have any immediate questions or concerns, please contact your Takeda OnePath® Patient Support Manager at 866-888-0660. Patient Support Managers are available Monday through Friday 8:30 AM – 8:00 PM ET.

Enclosed for your reference is the full NATPARA Prescribing Information and Medication Guide. For additional medical information, please contact your healthcare provider.

We recognize the important medical need that NATPARA fills for patients like you who are living with chronic hypoparathyroidism. As we have communicated previously, this is a fluid situation and we continue to work with urgency, and with US regulatory authority oversight, to avoid supply disruptions for patients receiving NATPARA through the SUP. We could have updated information regarding NATPARA 100-mcg and NATPARA 75-mcg as soon as the week of December 21, 2020 and will keep you updated as soon as new information is available. We appreciate your patience as we work to address these issues.

Sincerely,



Cheryl Schwartz
Head of U.S. Rare Disease Business Unit

Daniel McNamara
Head of U.S. Patient Services

What is NATPARA® (parathyroid hormone) for Injection?

- NATPARA is a prescription parathyroid hormone used with calcium and vitamin D to control low blood calcium (hypocalcemia) in people with low parathyroid hormone blood levels (hypoparathyroidism).
- NATPARA is only for people who do not respond well to treatment with calcium and active forms of vitamin D alone, because it may increase the possible risk of bone cancer (osteosarcoma).
- NATPARA was not studied in people with hypoparathyroidism caused by calcium-sensing receptor mutations.
- NATPARA was not studied in people who get sudden hypoparathyroidism after surgery.
- It is not known if NATPARA is safe and effective for children 18 years of age and younger. NATPARA should not be used in children and young adults whose bones are still growing.

Important Safety Information

What is the most important information I should know about NATPARA?

Warning: Possible bone cancer (osteosarcoma).

- During animal drug testing, NATPARA caused some rats to develop a bone cancer called osteosarcoma. It is not known if people who take NATPARA will have a higher chance of getting osteosarcoma. Tell your doctor right away if you have pain in any areas of your body that does not go away, or any new or unusual lumps or swelling under your skin that is tender to touch.

- **NATPARA is only available through the NATPARA Risk Evaluation and Mitigation Strategy (REMS) Program.** The purpose of the NATPARA REMS program is to inform patients about the potential risk of osteosarcoma associated with the use of NATPARA. For more information about this REMS program, call 1-855-NATPARA (628-7272) or go to **www.NATPARAREMS.com.**

NATPARA may cause other serious side effects, including:

High blood calcium (hypercalcemia)

- NATPARA can cause some people to have a higher blood calcium level than normal.

1. Your doctor should check your blood calcium before you start and during your treatment with NATPARA.
2. Tell your doctor if you have nausea, vomiting, constipation, low energy, or muscle weakness. These may be signs that you have too much calcium in your blood.

Low blood calcium (hypocalcemia)

- People who stop using or miss a dose of NATPARA may have an increased risk of severe low blood calcium levels.
- Tell your doctor if you have tingling of your lips, tongue, fingers and feet, twitching of face muscles, cramping of feet and hands, seizures, depression, or have problems thinking or remembering.

Who should not use NATPARA?

- **Do not use NATPARA** if you are allergic to parathyroid hormone or any of the ingredients in NATPARA.

What should I tell my healthcare provider before using NATPARA?

- **Before you start using NATPARA, tell your doctor about all of your medical conditions. Tell your doctor about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

What are the possible side effects of NATPARA?

- **NATPARA may cause serious side effects like allergic (hypersensitivity) reaction, including anaphylaxis**. Tell

your healthcare provider or get emergency medical help right away if you have any of the following symptoms of an allergic reaction:

- swelling of your face, lips, mouth, or tongue
- breathing problems
- fainting, dizziness, feeling lightheaded (low blood pressure)
- fast heartbeat
- itching
- rash
- hives

- **The most common side effects of NATPARA include:** tingling, tickling, or burning feeling of the skin, low or high blood calcium, headache, nausea, reduced sense of touch or sensation, diarrhea, vomiting, pain in joints, too much calcium in urine, and pain in limbs.

Enclosure: NATPARA Full Prescribing Information

Date: November 16th, 2020

Dear Valued Patient,

We are writing to provide an update on the information we provided in October 2020 regarding the potential for a near-term supply interruption of NATPARA® (parathyroid hormone) for Injection that may impact U.S. patients receiving NATPARA 100-mcg through the Special Use Program. We are also notifying you that we are now anticipating a near-term supply interruption of NATPARA 25-mcg, as well.

As we communicated in October, we have been monitoring supply of NATPARA to prepare for potential supply interruptions. Based on our current assessments, we are anticipating supply interruptions for NATPARA 25-mcg, as early as **December 8, 2020**, as well as NATPARA 100-mcg as early as **January 2, 2021**.

If you are receiving NATPARA 25-mcg or NATPARA 100-mcg, please see the following time-sensitive information regarding the immediate actions you must take. If you are receiving other doses of NATPARA, there's nothing you need to do at this time. However, supply status updates for all other NATPARA doses are also included in this letter.

IMMEDIATE ACTION REQUIRED FOR PATIENTS RECEIVING NATPARA 25-MCG OR NATPARA 100-MCG
If you have not yet contacted your prescribing physician to determine the best treatment plan for you, please contact him/her as soon as possible. NATPARA 25-mcg is expected to be unavailable due to a supply interruption as soon as December 8, 2020, and NATPARA 100-mcg is expected to be unavailable due to a supply interruption as soon as January 2, 2021. Based on your prescriber's independent medical judgement, your revised treatment plan may require a new prescription. Please ensure you work closely with your prescribing physician on any changes to your treatment plan, including the potential for a new prescription.

Patient safety is Takeda's main priority and, as a patient enrolled in the Single Use Program who is receiving **NATPARA 25-mcg** or **NATPARA 100-mcg**, we are alerting you and your prescribing physician that any potential interruption or reduction in the daily dose of NATPARA can cause a sharp decrease in blood calcium levels (severe hypocalcemia) which can be dangerous. It is important for you to work closely with your healthcare provider for important medical recommendations, including frequent monitoring of your blood calcium levels and close titration of active vitamin D and calcium supplements if you stop or alter your dose as a result of this supply interruption to avoid hypocalcemia.

NO IMMEDIATE ACTION REQUIRED FOR PATIENTS RECEIVING NATPARA 50-mcg or NATPARA 75-mcg:
At this time, we do not anticipate near-term supply interruptions for **NATPARA 50-mcg** or **NATPARA 75-mcg** doses before the end of 2020. However, we are closely monitoring these NATPARA doses and could experience supply interruptions in the event that manufacturing disruptions persist. We are committed to supply continuity and will provide you and your prescribing physician with an update on all NATPARA doses by mid-December.

Compliance with Special Use Program Terms & Conditions
As a patient who is receiving NATPARA through the Special Use Program, we want to remind you that each NATPARA cartridge under the Special Use Program (single dose use) is intended for one use only,

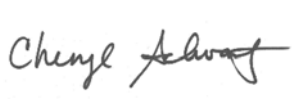
and that used cartridges with remaining product are to be returned to Takeda in accordance with the Special Use Program (single dose use) instructions. Non-compliance with the rules under the Special Use Program (single dose use) could result in termination of your ability to receive NATPARA product through the program.

OnePath will continue to work closely with your prescribing physician to support your treatment plan. If you have any immediate questions or concerns, please contact your Takeda OnePath® Patient Support Manager at 866-888-0660. Patient Support Managers are available Monday through Friday 8:30 AM – 8:00 PM ET.

Enclosed for your reference is the full NATPARA Prescribing Information and Medication Guide. For additional medical information, please contact your healthcare provider.

We recognize the important medical need that NATPARA fills for patients like you who are living with chronic hypoparathyroidism. While we focus on limiting these supply interruptions for patients who are receiving NATPARA through the Special Use Program, we continue to prioritize the goal of safely bringing NATPARA back to the broader patient community with U.S. Regulatory Authority oversight.

Sincerely,



Cheryl Schwartz
Head of U.S. Rare Disease Business Unit

Daniel McNamara
Head of U.S. Patient Services

What is NATPARA® (parathyroid hormone) for Injection?

- NATPARA is a prescription parathyroid hormone used with calcium and vitamin D to control low blood calcium (hypocalcemia) in people with low parathyroid hormone blood levels (hypoparathyroidism).
- NATPARA is only for people who do not respond well to treatment with calcium and active forms of vitamin D alone, because it may increase the possible risk of bone cancer (osteosarcoma).
- NATPARA was not studied in people with hypoparathyroidism caused by calcium-sensing receptor mutations.
- NATPARA was not studied in people who get sudden hypoparathyroidism after surgery.
- It is not known if NATPARA is safe and effective for children 18 years of age and younger. NATPARA should not be used in children and young adults whose bones are still growing.

Important Safety Information
What is the most important information I should know about NATPARA?
Warning: Possible bone cancer (osteosarcoma).

- During animal drug testing, NATPARA caused some rats to develop a bone cancer called osteosarcoma. It is not known if people who take NATPARA will have a higher chance of getting osteosarcoma. Tell your doctor right away if you have pain in any areas of your body that does not go away, or any new or unusual lumps or swelling under your skin that is tender to touch.

- **NATPARA is only available through the NATPARA Risk Evaluation and Mitigation Strategy (REMS) Program.** The purpose of the NATPARA REMS program is to inform patients about the potential risk of osteosarcoma associated with the use of NATPARA. For more information about this REMS program, call 1-855-NATPARA (628-7272) or go to **www.NATPARAREMS.com.**

NATPARA may cause other serious side effects, including:

High blood calcium (hypercalcemia)

- NATPARA can cause some people to have a higher blood calcium level than normal.

1. Your doctor should check your blood calcium before you start and during your treatment with NATPARA.
2. Tell your doctor if you have nausea, vomiting, constipation, low energy, or muscle weakness. These may be signs that you have too much calcium in your blood.

Low blood calcium (hypocalcemia)

- People who stop using or miss a dose of NATPARA may have an increased risk of severe low blood calcium levels.
- Tell your doctor if you have tingling of your lips, tongue, fingers and feet, twitching of face muscles, cramping of feet and hands, seizures, depression, or have problems thinking or remembering.

Who should not use NATPARA?

- **Do not use NATPARA** if you are allergic to parathyroid hormone or any of the ingredients in NATPARA.

What should I tell my healthcare provider before using NATPARA?

- **Before you start using NATPARA, tell your doctor about all of your medical conditions. Tell your doctor about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

What are the possible side effects of NATPARA?

- **NATPARA may cause serious side effects like allergic (hypersensitivity) reaction, including anaphylaxis**. Tell your healthcare provider or get emergency medical help right away if you have any of the following symptoms of an allergic reaction:
  - swelling of your face, lips, mouth, or tongue
  - breathing problems
  - fainting, dizziness, feeling lightheaded (low blood pressure)
  - fast heartbeat
  - itching
  - rash
  - hives

- **The most common side effects of NATPARA include:** tingling, tickling, or burning feeling of the skin, low or high blood calcium, headache, nausea, reduced sense of touch or sensation, diarrhea, vomiting, pain in joints, too much calcium in urine, and pain in limbs.

Enclosure: NATPARA Full Prescribing Information

Dear Valued Patient,

As a patient who is receiving NATPARA® (parathyroid hormone) for Injection through the Special Use Program (SUP), we are writing to inform you of an anticipated near-term supply interruption of **NATPARA 100-mcg** as early as **November 21st, 2020**.

If you are receiving NATPARA 100-mcg, please see the following time-sensitive information regarding the immediate actions you must take. If you are receiving other doses of NATPARA, there's nothing you need to do at this time. However, supply status updates for all other NATPARA doses are also included in this letter.

IMMEDIATE ACTION REQUIRED FOR PATIENTS RECEIVING NATPARA 100-mcg:
Please contact your prescribing physician as soon as possible to determine the best treatment plan for you. Based on your prescriber's independent medical judgement, your revised treatment plan may require a new prescription. Please ensure you work closely with your prescribing physician on any changes to your treatment plan, including the potential for a new prescription.

These supply interruptions were caused by unexpected manufacturing disruptions and are separate from the issue of rubber particulates originating from the rubber septum of the NATPARA cartridge. We deeply regret the interruption in supply and are making it a priority to bring product back quickly. At the same time, we are working on possible options for alternate treatment approaches with U.S. Regulatory Authority (U.S. Food & Drug Administration or "FDA") oversight and will keep you and your prescribing physician informed.

Patient safety is Takeda's main priority and, as a patient enrolled in the Single Use Program who is receiving **NATPARA 100-mcg**, we are alerting you and your prescribing physician that any potential interruption or reduction in the daily dose of NATPARA can cause a sharp decrease in blood calcium levels (severe hypocalcemia) which can be dangerous. It is important for you to work closely with your healthcare provider for important medical recommendations, including frequent monitoring of your blood calcium levels and close titration of active vitamin D and calcium supplements if you stop or alter your dose as a result of this supply interruption to avoid hypocalcemia.

NO IMMEDIATE ACTION REQUIRED FOR PATIENTS RECEIVING NATPARA 25-mcg, NATPARA 50-mcg or NATPARA 75-mcg:
At this time, we **do not** anticipate near-term supply interruptions for **NATPARA 25-mcg**, **NATPARA 50-mcg** or **NATPARA 75-mcg** doses. However, we are closely monitoring these NATPARA doses and could experience supply interruptions in the event that manufacturing disruptions persist. We are committed to supply continuity and will provide you and your prescribing physician with an update on the **NATPARA 25-mcg**, **NATPARA 50-mcg** and **NATPARA 75-mcg** doses by November 16, 2020.

Compliance with Special Use Program Terms & Conditions
As a patient who is receiving NATPARA through the Special Use Program, we want to remind you that each NATPARA cartridge under the Special Use Program (single dose use) is intended for one use only, and that used cartridges with remaining product are to be returned to Takeda in accordance with the Special Use Program (single dose use) instructions. Non-compliance with the rules under the Special Use

Program (single dose use) could result in termination of your ability to receive NATPARA product through the program.

OnePath will be working closely with your prescribing physician to support your treatment plan. For patients receiving NATPARA 100-mcg, a Takeda OnePath representative will also be reaching out to you in the coming days to walk you through this update and align on next steps. If you have any immediate questions or concerns, please call OnePath at 866-888-0660 Monday through Friday 8:30 AM – 8:00 PM ET.

Enclosed for your reference is the full NATPARA Prescribing Information and Medication Guide. For additional medical information, please contact your healthcare provider.

We recognize the important medical need that NATPARA fills for patients like you who are living with chronic hypoparathyroidism. While we focus on limiting these supply interruptions for patients who are receiving NATPARA through the Special Use Program, we continue to prioritize the goal of safely bringing NATPARA back to the broader patient community with U.S. Regulatory Authority oversight.

Sincerely,

Cheryl Schwartz
Head of U.S. Rare Disease Business Unit

Daniel McNamara
Head of U.S. Patient Services

What is NATPARA® (parathyroid hormone) for Injection?

- NATPARA is a prescription parathyroid hormone used with calcium and vitamin D to control low blood calcium (hypocalcemia) in people with low parathyroid hormone blood levels (hypoparathyroidism).
- NATPARA is only for people who do not respond well to treatment with calcium and active forms of vitamin D alone, because it may increase the possible risk of bone cancer (osteosarcoma).
- NATPARA was not studied in people with hypoparathyroidism caused by calcium-sensing receptor mutations.
- NATPARA was not studied in people who get sudden hypoparathyroidism after surgery.
- It is not known if NATPARA is safe and effective for children 18 years of age and younger. NATPARA should not be used in children and young adults whose bones are still growing.

Important Safety Information
What is the most important information I should know about NATPARA?
Warning: Possible bone cancer (osteosarcoma).

- During animal drug testing, NATPARA caused some rats to develop a bone cancer called osteosarcoma. It is not known if people who take NATPARA will have a higher chance of getting osteosarcoma. Tell your doctor right away if you have pain in any areas of your body that does not go away, or any new or unusual lumps or swelling under your skin that is tender to touch.

- **NATPARA is only available through the NATPARA Risk Evaluation and Mitigation Strategy (REMS) Program.** The purpose of the NATPARA REMS program is to inform patients about the potential risk of osteosarcoma associated with the use of NATPARA. For more information about this REMS program, call 1-855-NATPARA (628-7272) or go to **www.NATPARAREMS.com.**

NATPARA may cause other serious side effects, including:

High blood calcium (hypercalcemia)

- NATPARA can cause some people to have a higher blood calcium level than normal.

1. Your doctor should check your blood calcium before you start and during your treatment with NATPARA.
2. Tell your doctor if you have nausea, vomiting, constipation, low energy, or muscle weakness. These may be signs that you have too much calcium in your blood.

Low blood calcium (hypocalcemia)

- People who stop using or miss a dose of NATPARA may have an increased risk of severe low blood calcium levels.
- Tell your doctor if you have tingling of your lips, tongue, fingers and feet, twitching of face muscles, cramping of feet and hands, seizures, depression, or have problems thinking or remembering.

Who should not use NATPARA?

- **Do not use NATPARA** if you are allergic to parathyroid hormone or any of the ingredients in NATPARA.

What should I tell my healthcare provider before using NATPARA?

- **Before you start using NATPARA, tell your doctor about all of your medical conditions. Tell your doctor about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

What are the possible side effects of NATPARA?

- **NATPARA may cause serious side effects like allergic (hypersensitivity) reaction, including anaphylaxis**. Tell your healthcare provider or get emergency medical help right away if you have any of the following symptoms of an allergic reaction:
  - swelling of your face, lips, mouth, or tongue
  - breathing problems
  - fainting, dizziness, feeling lightheaded (low blood pressure)
  - fast heartbeat
  - itching
  - rash
  - hives

- **The most common side effects of NATPARA include:** tingling, tickling, or burning feeling of the skin, low or high blood calcium, headache, nausea, reduced sense of touch or sensation, diarrhea, vomiting, pain in joints, too much calcium in urine, and pain in limbs.

Enclosure: NATPARA Full Prescribing Information

September 25, 2019

Dear Valued Patient,

We recognize that the NATPARA® recall in the US has been extremely difficult for patients, their families and caregivers. Since this began on September 5, 2019, our team has been working diligently with the FDA on a number of potential solutions to bring this critical medicine back to patients.

While we are in discussions with the FDA to reintroduce NATPARA to the broader patient community, Takeda and the FDA have developed a Special Use Program for NATPARA. The program is intended to support patients previously prescribed NATPARA who are facing life-threatening complications as a result of discontinuation of NATPARA, despite efforts to actively manage their condition. Through this program, healthcare providers will be able to request NATPARA for patients facing life-threatening complications.

It is anticipated that an extremely small number of patients prescribed NATPARA may be eligible for this limited program. Additional information about the Special Use Program for healthcare providers can be found here: https://www.takeda.com/en-us/newsroom/news-releases/2019/takeda-announces-natpara-special-use-program-in-the-us/. Physicians are also receiving detailed information about this new program.

Patients who have questions about their eligibility under the Special Use Program or about their individual treatment plans should consult with their NATPARA prescribing physician.

While this is an important first step, we realize this short-term and extremely limited program will not address the needs of the vast majority of patients. We have heard your frustration and want to assure you that we are working diligently with the FDA on both short-term and long-term solutions to bring NATPARA back to the broader patient community, which remains our highest priority.

We are dedicated to the hypoparathyroidism community and the resupply of NATPARA for patients. We will continue to work with the FDA on this issue and keep patients and healthcare providers informed as more information becomes available.

As always, our OnePath® team is available to support you. Please reach out to a OnePath team member at 1-866-888-0660, Monday through Friday 8:30 a.m. to 8:00 p.m. ET.

Sincerely,

Dan McNamara
Head of US Patient Services

Shire-NPS Pharmaceuticals, Inc., part of the Takeda Group
300 Shire Way
Lexington, MA 02421
USA

What is NATPARA® (parathyroid hormone) for Injection?

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- NATPARA was not studied in people with hypoparathyroidism caused by calcium-sensing receptor mutations.
- NATPARA was not studied in people who get sudden hypoparathyroidism after surgery.
- It is not known if NATPARA is safe and effective for children 18 years of age and younger. NATPARA should not be used in children and young adults whose bones are still growing.

Important Safety Information

What is the most important information I should know about NATPARA?

Warning: Possible bone cancer (osteosarcoma).

- During animal drug testing, NATPARA caused some rats to develop a bone cancer called osteosarcoma. It is not known if people who take NATPARA will have a higher chance of getting osteosarcoma. Tell your doctor right away if you have pain in any areas of your body that does not go away, or any new or unusual lumps or swelling under your skin that is tender to touch.
- **NATPARA is only available through the NATPARA Risk Evaluation and Mitigation Strategy (REMS) Program.** The purpose of the NATPARA REMS program is to inform patients about the potential risk of osteosarcoma associated with the use of NATPARA. For more information about this REMS program, call 1-855-NATPARA (628-7272) or go to **www.NATPARAREMS.com.**

NATPARA may cause other serious side effects, including:

High blood calcium (hypercalcemia)

- NATPARA can cause some people to have a higher blood calcium level than normal.
  - Your doctor should check your blood calcium before you start and during your treatment with NATPARA.
  - Tell your doctor if you have nausea, vomiting, constipation, low energy, or muscle weakness. These may be signs that you have too much calcium in your blood.

Low blood calcium (hypocalcemia)

- People who stop using or miss a dose of NATPARA may have an increased risk of severe low blood calcium levels.
- Tell your doctor if you have tingling of your lips, tongue, fingers and feet, twitching of face muscles, cramping of feet and hands, seizures, depression, or have problems thinking or remembering.

Shire-NPS Pharmaceuticals, Inc., part of the Takeda Group
300 Shire Way
Lexington, MA 02421
USA

Who should not use NATPARA?

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What should I tell my healthcare provider before using NATPARA?

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What are the possible side effects of NATPARA?

- **NATPARA may cause serious side effects like allergic (hypersensitivity) reaction, including anaphylaxis**. Tell your healthcare provider or get emergency medical help right away if you have any of the following symptoms of an allergic reaction:
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  - fainting, dizziness, feeling lightheaded (low blood pressure)
  - fast heartbeat
  - itching
  - rash
  - hives

- **The most common side effects of NATPARA include:** tingling, tickling, or burning feeling of the skin, low or high blood calcium, headache, nausea, reduced sense of touch or sensation, diarrhea, vomiting, pain in joints, too much calcium in urine, and pain in limbs.

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

S52117 09/19

Shire-NPS Pharmaceuticals, Inc., part of the Takeda Group
300 Shire Way
Lexington, MA 02421
USA

Takeda Announces NATPARA® Special Use Program in the US

Takeda has worked with the FDA to develop a Special Use Program for NATPARA®. The program is intended to support patients previously prescribed NATPARA who are facing life-threatening complications as a result of discontinuation of NATPARA. Through this program, healthcare providers will be able to request NATPARA for these extraordinary, life-threatening cases. It is anticipated that an extremely small number of patients prescribed NATPARA will qualify for this very limited program. Additional information for healthcare providers about the Special Use Program can be found here. Patients who have questions about their eligibility under the Special Use Program or about their individual treatment plans should consult with their healthcare providers.

We realize that while this program is an important first step, it will only help a very small number of patients. We recognize that many more patients are in need of NATPARA to control their hypoparathyroidism. Takeda continues to work with the FDA on both short- and long-term solutions to bring NATPARA back to the broader patient community, which remains our highest priority.

We are committed to the hypoparathyroidism community and the safe supply of NATPARA. We will continue to work urgently on this issue and keep patients and healthcare providers informed of our progress in resuming supply.

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- Tell your doctor if you have tingling of your lips, tongue, fingers and feet, twitching of face muscles, cramping of feet and hands, seizures, depression, or have problems thinking or remembering.

Tell your doctor right away if you have any of these signs and symptoms of **high or low blood calcium** levels.

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- **Do not use NATPARA** if you are allergic to parathyroid hormone or any of the ingredients in NATPARA.

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- **Before you start using NATPARA, tell your doctor about all of your medical conditions. Tell your doctor about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

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- **The most common side effects of NATPARA include:** tingling, tickling, or burning feeling of the skin, low or high blood calcium, headache, nausea, reduced sense of touch or sensation, diarrhea, vomiting, pain in joints, too much calcium in urine, and pain in limbs.

These are not all the possible side effects of NATPARA. For more information, talk with your doctor.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit **www.fda.gov/medwatch** or call **1-800-FDA-1088**.

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