4th October 2022

Direct Healthcare Professional Communication (DHPC)

Natpar (parathyroid hormone (rDNA)) ▼ 100/75/50/25 micrograms/dose powder and solvent for solution for injection: Discontinuation of manufacturing at the end of 2024 and update on 100mcg shortage

Marketing Authorisation Number:
PLGB 54937/0009-0012
EU/1/15/1078/001-004

Dear Healthcare Professional,

Takeda UK Limited (acting on behalf of the Marketing Authorisation Holder, Takeda International AG Ireland Branch) in agreement with the Medicines and Healthcare products Regulatory Agency (MHRA) and European Medicines Agency (EMA) would like to inform you of the following:

Summary

- **Manufacturing of all strengths of Natpar will be discontinued globally at the end of 2024, due to unresolved manufacturing challenges. This means that Natpar will be withdrawn from the global market.**
- **Beyond 2024, Takeda intends to supply available doses until inventory is depleted or expired. Takeda will provide updates before the manufacturing end date and ahead of any further potential supply interruptions.**
- **A shortage of the 100 mcg/dose strength will continue until the discontinuation of manufacturing. Healthcare professionals can prescribe an alternative dosing regimen of Natpar, as per their clinical judgment (see details below).**
- **When changing the dosing or discontinuing Natpar, it is essential to closely monitor serum calcium levels and to monitor patients for signs and symptoms of hypocalcemia, while carefully adjusting active vitamin D and supplemental calcium doses in all patients.**
- **Healthcare professionals are advised not to initiate any new patients on any strength of Natpar.**

Background on the concern

Natpar is indicated as adjunctive treatment of adult patients with chronic hypoparathyroidism who cannot be adequately controlled with standard therapy alone.

Takeda has decided to discontinue manufacturing of all strengths of Natpar from the end of 2024 due to unresolved manufacturing issues.

The 100 mcg/dose strength shortage will continue until the discontinuation of manufacturing.

Takeda will provide updates before the manufacturing end date in late 2024 and ahead of any potential supply interruptions.

Alternative dosing options for patients already on Natpar 100 micrograms/dose, remain unchanged since our communication dated May 2022:

- Multiple dosing: If HCPs believe, in their independent clinical judgement, a 100 micrograms dose is necessary for their patients, they can prescribe two separate injections of Natpar 50 micrograms/dose. If the HCP decides to prescribe 2 consecutive doses of Natpar 50 micrograms/dose, the second dose should be administered in the contralateral thigh using a new needle within 15 minutes of the first dose. HCPs should consider monitoring of serum calcium levels and adjustment, as necessary, of exogenous calcium and/or active vitamin D.

  Or

- Reduced dosing: Natpar 75 micrograms/dose remains available for whom, in the HCP's independent clinical judgement, a reduced dose of Natpar 75 micrograms is appropriate. HCPs should consider monitoring of serum calcium levels and adjustment, as necessary, of exogenous calcium and/or active vitamin D.

It is imperative that the attached patient information, *'Patient/Caregiver Injection Instructions for Natpar 100 micrograms/dose shortage'* is given to the patient and that the patient is sufficiently educated. HCPs should go through the patient education materials with the patient, to make sure they are understood.

For patients receiving 2 x Natpar 50 micrograms/dose, make sure to communicate the following:
One dose of Natpar 50 micrograms/dose should be injected in each thigh. A new needle should be used for each injection and the dose indicator checked to confirm two doses of 50 mcg have been administered. To reduce the chance of local reactions, the injections should alternate between upper and lower parts of the thighs each day. The two doses should be taken less than 15 minutes apart; however if the patient by error takes only one dose, they should take the second dose as soon as possible and contact their doctor. The patient must be educated on the importance of correct dosing, and to contact the HCP in case of any error in dosing.

For patients where the dose is reduced from Natpar 100 micrograms/day to Natpar 75 micrograms/day, make sure to communicate the following:
The reduction in dose places the patient at increased risk of hypocalcemia. This must be communicated to the patient, informing them of the signs of hypocalcaemia and on when they should inform their doctor.

For all patients affected by the drug shortage:
It is very important to closely monitor serum calcium levels and observe for signs and symptoms of hypocalcemia while carefully adjusting active vitamin D and supplemental calcium doses in any patient

affected by the Natpar 100 micrograms/dose shortage. Please review the SmPC Section 4.2 (Interruption or discontinuation of treatment) and Section 4.4 (Warnings and Precautions: Hypocalcemia).

No new patients on Natpar:
The manufacturing of all strengths of Natpar will be discontinued at the end of 2024. In order to ensure that existing patients can continue to receive treatment, HCPs are asked not to initiate any new patients **on any strength of Natpar**.

Call for reporting

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. When reporting, please provide as much information as possible including information about batch details, medical history, any concomitant medication, onset and treatment dates.

Please report suspected adverse reactions with any medicine or vaccine to the MHRA through the Yellow Card Scheme.

You can report via:

- the Yellow Card website: www.mhra.gov.uk/yellowcard
- the free Yellow Card app available from the Apple App Store or Google Play Store
- some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank) for healthcare professionals.

Alternatively, you can report a suspected side effect to the Yellow Card scheme by calling 0800 731 6789 for free, Monday to Friday between 9am and 5pm.

Adverse events should also be reported to Takeda: AE.GBR-IRL@takeda.com

Company Contact Point
For questions relating to the content of this communication please contact the Takeda Medical Information Department:

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