Zorginstituut Nederland

> Return address PO Box 320, 1110 AH Diemen

Director of Pharmaceuticals and Medical Technology at the Ministry of Health, Welfare and Sport
PO Box 20350
2500 EJ THE HAGUE

National Health Care Institute
Care
Medicinal Products

Willem Dudokhof 1
1112 ZA Diemen
PO Box 320
1110 AH Diemen
www.zorginstituutnederland.nl
info@zinl.nl

T +31 (0)20 797 85 55

Contact
Ms. N. Stam
T +31 (0)6 342 207 90

2022042285

Our reference
2022042285

Date 2 November 2022
Regarding Progress of the conditional inclusion process for rhPTH 1-84 (Natpar®)

Dear Ms van Rooijen,

Based on our advice of 6 October 2021, your predecessor has conditionally admitted recombinant human parathyroid hormone 1-84 (rhPTH 1-84) (Natpar®) to the basic health care package of the Health Insurance Act (Zvw) as an adjunctive treatment for adult patients with chronic hypoparathyroidism whose condition cannot be adequately controlled with standard therapy alone. This applies for the period of 1 November 2021 to 31 December 2024. Based on new developments, the National Health Care Institute advises you on the continuation of this conditional inclusion process.

Course of the procedure
Since the start of the conditional inclusion process, 20 Dutch patients have been treated with rhPTH 1-84. At the start of the process, a total of 100 Dutch patients were expected to be eligible for treatment with rhPTH 1-84. Data from the treated patients have been collected in a register (secondary supporting registry-based study: Natpar Monitor). During the sounding boardmeeting, the practitioners indicated that their patients benefit from the use of rhPTH 1-84. In addition, the international main study, which was part of the research proposal for conditional inclusion, has already been completed. The outcomes of this international study are expected to be published in the coming year.

Production issues
At the end of April 2022, marketing authorisation holder Takeda announced that the highest dose of rhPTH 1-84 (100 micrograms/dose) could not be delivered from the end of June 2022 due to production issues. It was also advised not to treat new patients. The duration of the production issues was unknown. On 4 October 2022, Takeda announced that the production issues cannot be solved and that production will therefore be discontinued worldwide at the end of 2024.

Consequences
The purpose of the conditional inclusion is to collect additional information on the effectiveness and appropriate use, to determine the package eligibility of the medicinal product concerned. Since Takeda will permanently stop production of rhPTH 1-84 at the end of 2024 and no new patients will be treated with it, rhPTH

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1-84 will not be able to enter the basic health care package at the end of the conditional inclusion. Therefore, the National Health Care Institute will not carry out a final assessment. This could be a reason to stop the conditional inclusion process of rhPTH 1-84. However, the National Health Care Institute has considered the following.

During the sounding board group meeting, the professional group indicated that it will endeavour next year to switch all patients who are currently taking rhPTH 1-84 to an alternative product. Since rhPTH 1-84 fulfilled an unmet medical need, there are currently no adequate alternatives available (yet). Therefore, patients will most likely experience symptoms due to dysregulation. For this reason, the practitioners and the patients may want to determine together the best time for the switch to an alternative. Patients are likely to switch to teriparatide as far as *off-label* use is concerned. However, the 2015 European hypoparathyroidism treatment guideline does not recommend treatment with teriparatide. In addition, it will be examined whether patients can be included in studies in which new treatments for hypoparathyroidism are being researched.

The National Health Care Institute therefore advocates offering practitioners and patients sufficient room to switch to an alternative. It is important to emphasize that patients are being forced to switch to another medicinal product due to production issues, not because of a lack of effectiveness of rhPTH 1-84. There are 20 patients who are probably going to be treated with rhPTH 1-84 for a maximum of one year.

Advice from the National Health Care Institute
Based on the above considerations, the National Health Care Institute recommends that the conditional inclusion process for rhPTH 1-84 be continued until all Dutch patients who are currently being treated with rhPTH 1-84 have responsibly switched to an alternative. Furthermore, no new patients should be treated with rhPTH 1-84. The National Health Care Institute will inform the involved parties about this.

Yours sincerely,

Peter Siebers
Acting Chairperson of the Executive Board