Zorginstituut Nederland

Return address PO Box 320, 1110 AH Diemen

To the Minister of Medical Care
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
warcg@zinl.nl

2024004174

Our reference
2024004174

Date 21 February 2024
Re: Advice on the early discontinuation of the conditional inclusion of medicinal products rhPTH 1-84 (Natpar®) and ataluren (Translarna®)

Dear Ms Dijkstra,

Based on our advice, your predecessor conditionally included recombinant human parathyroid hormone 1-84 (rhPTH 1-84) (Natpar®) to the basic health care package of the Health Insurance Act (Zvw) as a complementary treatment for adult patients with chronic hypoparathyroidism whose condition cannot be adequately controlled by standard therapy. This applies for the period of 1 November 2021 to 31 December 2024. In addition, from 1 November 2021 until 1 October 2024, your predecessor conditionally included ataluren (Translarna®) in the basic health care package for the treatment of Duchenne muscular dystrophy caused by a nonsense mutation in the dystrophin gene (nmDMD), in ambulatory patients aged two years and older. Based on new developments, the National Health Care Institute advises you on the early discontinuation of both conditional inclusion procedures.

rhPTH 1-84 CI procedure course
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. Takeda also recommended not to treat new patients. On 4 October 2022, Takeda announced that the production issues could not be resolved and that the production of rhPTH 1-84 in all dosages would therefore be discontinued worldwide at the end of 2024. Due to this termination of production, the National Health Care Institute will not carry out a package assessment.

The National Health Care Institute advised you (in November 2022) to continue the CI procedure until all Dutch patients treated with rhPTH 1-84 have been responsibly switched to an alternative.[1] Since rhPTH 1-84 fulfilled an *unmet medical need*, no adequate alternatives were available (yet). Patients were expected to suffer effects and experience associated symptoms. Therefore, the National Health Care Institute advocated giving physicians and patients enough room to switch to an alternative so that they could jointly decide the most suitable moment. Patients could be switched back to the standard treatment with calcium and/or vitamin D that had previously provided inadequate control. Patients could

[1] https://www.zorginstituutnederland.nl/publicaties/adviezen/2022/11/02/voortgang-voorwaardelijk-toelatingstraject-van-rhpth-1-84-natpar

National Health Care Institute
Care
Medicinal Products

Date
21 February 2024

Our reference
2024004174

also be switched to *off-label* teriparatide, although this is not recommended in the European hypoparathyroidism treatment guideline of 2015. In addition, patients could potentially be included in studies in which new treatments for hypoparathyroidism are being researched. Finally, the National Health Care Institute, like the EMA, recommended that no new patients be treated with rhPTH 1-84.

At present, 3 patients are still being treated with rhPTH 1-84. Physicians have indicated that they want to continue to treat these patients with rhPTH 1-84 for as long as possible. However, the National Health Care Institute assumes that physicians and patients have now been given sufficient additional time to discontinue treatment with rhPTH 1-84 and switch to an alternative.

Ataluren CI process course
On 31 July 2023, the National Health Care Institute advised you to change the end date of the CI procedure of ataluren from 1 February 2024 to 1 October 2024.[2] This 8-month extension was recommended due to delay in the advice of the *Committee for Medicinal Products for Human Use* (CHMP) and the modification of the criteria for exemption from a pharmacoeconomic (PE) analysis by the National Health Care Institute. This advice was adopted by your predecessor on 30 August 2023.

On 15 September 2023, the CHMP recommended not to renew the market authorisation of ataluren based on, among other things, the results of the double-blind phase of the 041 study (main study for the CI) that showed a lack of effectiveness for ataluren. On 4 October 2023, the marketing authorisation holder for ataluren requested a re-evaluation of the CHMP advice. On 26 January 2024, the CHMP decided definitively not to renew the market authorisation of ataluren. This means that if the European Commission adopts the CHMP advice, ataluren will be withdrawn from the European market. The National Health Care Institute will therefore not carry out a package assessment of ataluren.

Advice from the National Health Care Institute
Based on the above considerations, the National Health Care Institute recommends that the CI procedure for rhPTH 1-84 be terminated early. The National Health Care Institute also recommends the early discontinuation of the CI procedure for ataluren as soon as the European Commission adopts the CHMP advice. The National Health Care Institute will inform the stakeholders about the early discontinuation of both CI procedures.

As set out in the exit strategy of the covenant for both CI procedures, the reimbursement of rhPTH 1-84 and ataluren will stop at the moment the CI procedure is discontinued (early). The National Health Care Institute would like to stress that the marketing authorisation holder for rhPTH 1-84 is allowed to make the medicinal product available (free of charge) to the 3 patients still being treated with it until production is permanently discontinued at the end of 2024. As ataluren is withdrawn from the European market, the marketing authorisation holder will stop supplying the medicinal product to patients and therefore treatment must be discontinued. There are currently no new treatment options for patients with Duchenne. The National Health Care Institute understands that this

[2] https://www.zorginstituutnederland.nl/publicaties/adviezen/2023/07/31/advies---verleng-voorwaardelijk-toelatingstraject-ataluren-translarna

is a disappointing situation for patients, but is confident that patients will be informed as best as possible by their physicians about further health care/treatment.

Yours sincerely,

Sjaak Wijma
Chairperson of the Executive Board

National Health Care Institute
Care
Medicinal Products

Date
21 February 2024

Our reference
2024004174