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Our reference
2022021244

Date 8 July 2022
Subject GVS advice on setmelanotide (Imcivree®)

Dear Dr Kuipers,

In his letter of 5 January 2022 (reference CIBG-21-03111), your predecessor asked the National Health Care Institute to carry out a substantive assessment of whether the medicinal product setmelanotide (Imcivree®) is interchangeable with a product that is included in the Medicine Reimbursement System (GVS). The National Health Care Institute, advised by the Scientific Advisory Board (WAR), has now completed this assessment.

Setmelanotide (Imcivree®) is indicated for the treatment of obesity and the control of hunger associated with genetically confirmed loss-of-function biallelic pro-opiomelanocortin deficiency (POMC deficiency), including PCSK1 deficiency, or biallelic leptin receptor deficiency (LEPR deficiency) in adults and in children 6 years of age and above.

The marketing authorisation holder is asking that the entire registered indication be included on List 1B of the Healthcare Insurance Regulations.

Outcomes of the substantive assessment

Review of interchangeability
To determine the place of a medicinal product in the GVS, its interchangeability with medicinal products already included in the GVS must first be assessed. Based on the criteria for interchangeability, setmelanotide (Imcivree®) is not interchangeable with other medicinal products included in the GVS.

Therapeutic value
The indicated population (POMC-deficient and LEPR-deficient adults and children 6 years of age and above) suffers from a severe and extremely rare form of genetic obesity. Aside from the intensive combined lifestyle intervention (CLI+), no standard treatment is available at the present time. According to clinical experts, CLI+ has virtually no effect on weight in POMC-deficient and LEPR-deficient patients. The current treatment cannot achieve a clinically relevant weight reduction in terms of the *Body Mass Index* (BMI). As a result, the extremely

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elevated weight-related health risk cannot be reduced. Thus, there is a great need for specific pharmacotherapy for this small group of patients. In two setmelanotide studies, a clinically relevant effect on weight reduction was achieved in patients with POMC deficiency and LEPR deficiency. This effect appears to persist for a lengthy period of time. The most common undesirable effects are pigmentation spots and injection site reactions. In addition, the POMC study and the LEPR study included reports of depression and suicidal ideation. It is not known whether these undesirable effects are related to treatment with setmelanotide or whether they are inherent to the disorder itself.
Setmelanotide complies with established medical science and medical practice as an adjunct to the intensive combined lifestyle intervention (CLI+) in adults and in children 6 years of age and above with genetically confirmed POMC deficiency or LEPR deficiency. The National Health Care Institute concludes that the medicinal product has added value compared to the usual care.

Budget impact analysis (BIA)
Setmelanotide treatment costs €250,938 per patient per year. Taking account of assumptions about the exact number of patients with this disorder, the proportion of patients who will discontinue treatment, the exact dosage that patients can tolerate, and patient compliance, inclusion in the GVS is expected to be accompanied by additional costs to the pharmaceutical budget of approximately €2.1 million in the third year after inclusion in the basic health care package.

Pharmaco-economic analysis
Based on the estimated budget impact, the product is exempt from pharmaco-economic analysis. That is largely because of the very limited number of patients. At the same time, the National Health Care Institute calls attention to the high annually recurring costs per patient. As in previous comparable situations, the National Health Care Institute will also keep this case in mind when evaluating the criteria for conducting future pharmaco-economic analyses. In addition, the National Health Care Institute deems it appropriate for health care insurers to reach competitive purchase agreements for setmelanotide.

Advice
The National Health Care Institute advises you to include setmelanotide (Imcivree®) in List 1B of the GVS, with the following reimbursement condition:
Only for an insured person aged six years or above:

- With genetically confirmed (according to international genetic classification standards) pro-opiomelanocortin (POMC) deficiency, including proprotein convertase subtilisin/kexin type 1 (PCSK1) deficiency, or biallelic leptin receptor (LEPR) deficiency
- Who have undergone a combined lifestyle intervention
- Treatment should be discontinued if, after 6 months at the maintenance dosage, the initial weight in growing children has not stabilized or if it has not decreased by at least 5% in mature adolescents and adults.
- The treatment should be carried out by a centre of expertise.

Yours sincerely,

Sjaak Wijma
Chairperson of the Executive Board

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