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Our reference
2022014655

Date 16 May 2022
Re: GVS advice GLP-1 receptor agonists extension further conditions

Dear Mr Kuipers,

In your letter of 31 January 2022 (CIBG-22-03252), you asked the National Health Care Institute to assess whether the further conditions of the GLP-1 agonists could be extended. This is a group assessment. The National Health Care Institute has now completed this assessment following advice from the Scientific Advisory Board (WAR). The considerations are included in the report attached to this letter.

Background
In the Netherlands, there are seven glucagon-like peptide-1 (GLP-1) agonists on the market: dulaglutide (Trulicity®), exenatide (Byetta® and Bydureon®), liraglutide (Victoza® and Saxanda®), lixisenatide (Lyxumia®) and semaglutide (Ozempic® and Rybelsus®). Rybelsus® is available in the form of a tablet and the other GLP1 receptor agonists are available in the form of a subcutaneous injection (under the skin).

The guideline on the treatment of diabetes mellitus type 2 (DM2) has been revised recently by the Dutch College of General Practitioners (NHG). Based on this revision, the further conditions of the SGLT-2 inhibitors have recently been extended after a group assessment. In consultation with the stakeholders in the Round Table for Diabetes Care, marketing authorisation holders of the GLP1 agonists have also jointly submitted a file which combines the available knowledge on the application of these products.

The indication to be assessed is for patients with diabetes mellitus type 2 (DM2) and a very high risk of cardiovascular disease where glucose levels cannot be adequately regulated with a SGLT-2 inhibitor or if the use of a SGLT-2 inhibitor is contraindicated.

The GLP1 receptor agonists are placed in a cluster on List 1A and on List 2 of the Health Insurance Regulation. This means that the reimbursement of these medicinal products is limited to the patient groups covered by the conditions formulated in Annex 2:

1. only for insured persons with diabetes mellitus type 2 and a BMI ≥ 35 kg/m² whose blood glucose levels cannot be adequately regulated with the combination of metformin and a sulphonyl urea derivative at the

maximum tolerable dosages, and who do not use insulin; for *exenatide and liraglutide, the additional condition is:* unless the insured person is already being treated with this medicinal product in combination with insulin on 1 May 2011,

2. as an addition to metformin and basal insulin (NPH insulin/long-acting analogue insulin) for an insured person with diabetes mellitus type 2 and a BMI ≥ 30 kg/m^2 whose blood glucose values are insufficiently regulated after ≥ 3 months of treatment with optimal titrated basal insulin in combination with metformin (whether or not with a sulphonyl urea derivative) in a maximum tolerable dosage.

The further condition for liraglutide has also recently been extended with:

3. in combination with a combined lifestyle intervention (CLI) recognized by the RIVM, for the treatment of adults without diabetes mellitus type 2 with an extremely increased weight-related health risk and who are not (yet) eligible for metabolic surgery:
    a. with a BMI ≥35 kg/m^2 in combination with a comorbidity (cardiovascular disease, sleep apnoea and/or osteoarthritis) or
    b. With a BMI ≥40 kg/m^2.

    Treatment should be discontinued if after 3 months of using the maintenance dosage the initial weight has not decreased by at least 5%.

Outcome of the substantive assessment

Therapeutic value

The National Health Care Institute has concluded that the GLP1 receptor agonists dulaglutide (Trulicity®), liraglutide (Victoza®), exenatide (Byetta® and Bydureon®) and semaglutide (subcutaneous (Ozempic®) and oral (Rybelsus®)) meet the established medical science and medical practice in the treatment of adults with DM2 and a very high risk of cardiovascular disease. The National Health Care Institute concludes on the basis of the data that these medicinal products have an added value compared to only the standard treatment in patients with contraindications for an SGLT2 inhibitor. It can also be concluded that these products have added value in patients where glucose levels cannot be adequately regulated by the standard treatment consisting of at least an SGLT2 inhibitor and metformin. However, the evidence for this is more limited. The GLP1 receptor agonist lixisenatide (Lyxumia®) has no added value compared to the standard treatment in DM2 patients and a very high risk of cardiovascular disease, and therefore does not meet the established medical science and medical practice.

Budget impact analysis (BIA)

Treatment with a GLP1 receptor agonist costs € 1,122 per patient per year. Taking into account the assumptions about patient numbers, market penetration and patient compliance, extension of the reimbursement conditions for dulaglutide, exenatide, liraglutide and semaglutide in type 2 diabetes and a very high risk of cardiovascular disease are accompanied by additional costs charged to the pharmaceutical budget of at least €5.2 million up to a maximum of €5.7 million in the third year after inclusion in the basic insured package depending on the assumptions about market penetration.

Met opmerkingen [AVB1]: Vertaler: In het Nederlands: DM type 2, in het Engels Type 2 DM.

Pharmaco-economic analysis

Based on the estimated budget impact, the product is exempt from pharmaco-economic analysis.

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Advice
The National Health Care Institute advises you to extend the reimbursement conditions for dulaglutide, exenatide, liraglutide and semaglutide on the basis of the above considerations. The further condition for lixisenatide should not be extended. The proposed extension is accompanied by additional costs.

Extension of the further condition for dulaglutide, exenatide, liraglutide and semaglutide:
In addition to an SGLT2 inhibitor and metformin, or when an SGLT2 inhibitor is contraindicated, added to the standard treatment, for an insured person with diabetes mellitus type 2 with a very high risk of cardiovascular disease (according to the NHG guideline for Diabetes Mellitus type 2):

1. *With previously proven cardiovascular diseases; and/or*
2. *chronic kidney disease.*

Yours sincerely,

Sjaak Wijma
Chairperson of the Executive Board