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National Health Care Institute
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Our reference
2022014236

Date 17 May 2022
Subject GVS advice Mysimba

Dear Mr Kuipers,

In your letter of 28 February 2022 (reference CIBG-22-03447), you asked the National Health Care Institute to assess whether the product bupropion in combination with naltrexone (Mysimba®) can be included in the Medicine Reimbursement System (GVS). The National Health Care Institute has now completed the substantive assessment. The considerations are included in the GVS report attached to this letter, together with the pharmaco-therapeutic report and the budget impact analysis.

Mysimba® is indicated as an addition to a calorie-restricted diet and increased physical activity, for weight control in adult patients (≥ 18 years) with an initial Body Mass Index (BMI) of:
- 30 kg/m2 or more (obesity), or
- 27 kg/m2 to 30 kg/m2 (overweight) in the presence of one or more weight-related comorbidities (e.g., type 2 diabetes, dyslipidaemia or controlled hypertension).

It is available as a prolonged-release tablet. Contains per tablet: naltrexone (hydrochloride) 8 mg, bupropion (hydrochloride) 90 mg. The dose should be increased over a four-week period: *week 1:* 1 tablet in the morning, *week 2*: 1 tablet in the morning and 1 tablet in the evening, *week 3*: 2 tablets in the morning and 1 tablet in the evening *, week 4 and beyond*: 2 tablets in the morning and 2 tablets in the evening. This is also the maximum dosage. Treatment should be discontinued if the initial weight has not decreased by at least 5% after 16 weeks. The need to continue the treatment must be re-evaluated each year.

The market authorisation holder is asking for inclusion on List 1B of the Health Insurance Regulation.

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Outcome of the assessment

Review of interchangeability
The individual components of Mysimba® are already included in the GVS. On the basis of Article 2.40 (5) of the Health Insurance Regulation, Mysimba® can be included in List 1A in a new combination cluster.

Therapeutic value
Naltrexone/bupropion in addition to a combined lifestyle intervention (CLI) has added value compared to just CLI: the percentage of patients who achieve ≥5% and ≥10% weight reduction is greater, from a clinically relevant point of view, than in patients treated with CLI alone. The effect of naltrexone/bupropion on cardiometabolic risk factors and quality of life is (probably) not clinically relevant. It is still unclear whether treatment with naltrexone/bupropion leads to a clinically relevant increase in severe adverse effects. However, from a clinically relevant point of view there were more naltrexone/bupropion treated patients who discontinued therapy due to (gastrointestinal) side effects than patients with CLI alone.

The National Health Care Institute concludes that naltrexone/bupropion thus complies with the established medical science and medical practice for weight control in adult patients with obesity (BMI ≥30 kg/m2) or overweight patients (BMI 27 kg/m2 to 30 kg/m2 combined with one or more weight-related comorbidities) in addition to a combined lifestyle intervention (CLI).

Budget impact analysis (BIA)
4,237 patients are expected to be treated with naltrexone/bupropion in the third year after inclusion in the basic insured package. On this basis, inclusion in the GVS will be accompanied by additional costs charged to the pharmaceutical budget of approximately €3.7 million. Based on clinical studies, we have taken into account the fact that 50% of patients discontinue the trial treatment with naltrexone/bupropion due to insufficient effect (loss of body weight <5%). The cost per patient per year ranges from €396 for non-responders to €1,290 for patients treated for an entire year. It is still uncertain how long the treatment with naltrexone/bupropion will be continued.

As of 1 April, the medicinal product liraglutide (Saxenda®) has been included for some (approximately 10%) of the same patients, namely patients with an extremely increased weight-related health risk. The BIA does not take into account the substitution of liraglutide, since it cannot be ruled out that patients will switch to another treatment after failure.

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 recommends that naltrexone/bupropion (Mysimba®) be included in the GVS with the following reimbursement condition:

In combination with a combined lifestyle intervention (CLI) recognized by the RIVM, for the treatment of adults with:

- BMI ≥30 kg/m2 or
- BMI 27 kg/m2 to 30 kg/m2 in combination with a comorbidity ((risk factors) for cardiovascular disease, type 2 diabetes, sleep apnoea and/or osteoarthritis).

Treatment should be discontinued if, after 4 months of use, the initial weight has not decreased by at least 5%.

Yours sincerely,

Sjaak Wijma
Chairperson of the Executive Board