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Our reference
2022049988

Date 18 January 2023
Subject GVS advice odevixibat (Bylvay®)

Dear Mr Kuipers,

In your letter of 7 September 2022 (reference CIBG-22-04456), you asked the National Health Care Institute to carry out a substantive assessment of whether the medicinal product odevixibat (Bylvay®) 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 completed this assessment. The attached GVS report highlights the considerations in this respect.

Odevixibat (Bylvay®) is indicated for the treatment of progressive familial intrahepatic cholestasis (PFIC) in patients aged 6 months or older.

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

Outcome 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, odevixibat (Bylvay®) is not interchangeable with other medicinal products included in the GVS.

Therapeutic value
Progressive familial intrahepatic cholestasis (PFIC) is a group of rare, autosomal recessive (liver) disorders. In this condition, there are mutations in the genes that encode for transport proteins in the liver cells, resulting in insufficient excretion of bile acid. This causes cholestasis, which can lead to severe liver damage.
Pruritus (itching) is the most burdensome symptom of PFIC and often leads to scratching, which can cause severe cutaneous mutilation. This can also have a significant impact on daily activities and lead to, among other things, sleep deprivation, irritability, concentration disorders and reduced school results.

There is no pharmacological treatment with proven, sustainable effectiveness for PFIC. In the PEDFIC1 study, odevixibat was studied in patients 6 months or older with PFIC type 1 and 2.
Treatment with odevixibat results in a clinically relevant reduction of itching after 24 weeks of treatment. The itching showed a clinically relevant decrease in 55.1%

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of patients treated with odevixibat and in 30.1% of patients in the placebo arm. Odevixibat was also studied in an open-label extension study. There was no clinically relevant improvement of the itching for patients with a specific subtype (PFIC2 BSEP3). Therefore, patients with PFIC2 BSEP3 are excluded from reimbursement. There is no evidence that treatment with odevixibat results in a clinically relevant increase in the risk of intervention-related severe undesirable effects. Odevixibat complies with the established medical science and medical practice for the treatment of PFIC in patients aged 6 months or older, with the exception of patients with PFIC2 subtype BSEP3. The National Health Care Institute concludes, on the basis of the data, that odevixibathas an added value compared to the standard of care.

Budget impact analysis (BIA)
The National Health Care Institute currently estimates the prevalence of PFIC patients in the Netherlands at 26 and the number of newly diagnosed patients at 3 per year. Of the 26 prevalent patients, 16 are expected to be eligible for treatment with odevixibat. The estimated budget impact is therefore based on the treatment of 19 patients in the first year (16 prevalent and 3 newly diagnosed). Taking into account assumptions about patient numbers, response rates and treatment duration, the inclusion of odevixibat (Bylvay®) for PFIC on the GVS List 1B will be accompanied by additional costs charged to the pharmaceutical budget of from €3.9 to €5.1 million in the third year after inclusion. There is uncertainty about 1) the number of patients eligible for treatment, 2) the response rates of this new medicinal product, and 3) the dosage to be used.

Pharmaco-economic analysis
Based on the estimated budget impact, the product is exempt from a pharmaco-economic analysis. That is largely because of the very limited number of patients. However, the annual recurring costs per patient are high. 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 this context, the National Health Care Institute considers it desirable for health care insurers to make keen purchasing arrangements for odevixibat.

Advice
The National Health Care Institute advises to include odevixibat (Bylvay®) in List 1B of the GVS, with the following reimbursement conditions:
1. Only for an insured person aged six months or older
- with genetically confirmed PFIC (except PFIC2 subtype BSEP3);
- receiving treatment at a centre of expertise;
- who has not yet started non-invasive, symptomatic treatment, or has not resulted in a sustainable therapeutically satisfactory result.

2. Treatment should be discontinued if a clinically symptomatic treatment benefit is not demonstrated after a maximum of nine months of continuous treatment.

Yours sincerely,

Sjaak Wijma
Chairperson of the Executive Board