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Contact
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Date 24 March 2025
Re: GVS advice berotralstat (Orladeyo®) for hereditary angioedema

Our reference
2023050100

Dear Ms Agema,

The National Health Care Institute advises you on the inclusion of berotralstat (Orladeyo®) for the treatment of hereditary angioedema in the Medicine Reimbursement System (GVS). This advice was prompted by your request in the letter of 13 January 2025 (CIBG-24-07729).

Hereditary angioedema (HAE) is a hereditary disease in which a patient has attacks of swelling with a rapid onset. These swellings, also called oedema, can occur in various places in the body, for example in the skin, abdomen, throat or mouth. The swelling can be painful. Swelling in the mouth or throat can be life-threatening. In the treatment of HAE, a choice can be made between acute treatment of swellings and prophylactic treatment to prevent swellings.
The prevalence of HAE is estimated to be 1:50000. Based on declaration data, 230 patients were medically treated for HAE. 64 of them received routine prophylaxis.

Registered indication(s)
Berotralstat (Orladeyo®) is indicated for routine prevention of recurrent attacks of hereditary angioedema (HAE) in adult and adolescent patients aged 12 years and older.

It is available as an oral capsule (150 mg). The recommended dose is 150 mg berotralstat once daily for adults and adolescents aged 12 years and older weighing over 40 kg.

Claim by the marketing authorisation holder
Berotralstat (Orladeyo®) has at least an equal value for the registered indication to standard treatment with intravenous C1 esterase inhibitor (Cinryze®).

The marketing authorisation holder is requesting inclusion on List 1B of the Health Insurance Regulation.

Advice
The National Health Care Institute advises you to include berotralstat (Orladeyo®)

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for routine prevention of recurrent attacks of hereditary angioedema (HAE) in adult and adolescent patients aged 12 years and older in List 1B of the GVS. Inclusion is accompanied by savings for the pharmaceutical budget estimated at €1.6 million in year 3.

We explain the preparation of this advice below.

Substantive assessment

Assessment of interchangeability

Based on the criteria for interchangeability, the National Health Care Institute concluded that berotralstat is not interchangeable with other medicinal products included in the GVS. On this basis, berotralstat cannot be placed in List 1A. The National Health Care Institute has therefore assessed whether berotralstat can be included in List 1B.

Therapeutic value

Based on the indirect comparison of the placebo-controlled studies of berotralstat, C1 esterase inhibitors and lanadelumab in patients with HAE, it was concluded that the beneficial effects on the reduction of the number of attacks (and thus quality of life) and the adverse effects are similar. The National Health Care Institute concludes on the basis of this equal value that berotralstat meets the established medical science and medical practice.

Budget impact analysis

The National Health Care Institute estimates that 31 patients per year will be treated with berotralstat for this indication in year 3 after inclusion in the package. The total costs per patient per year are €146,365. This results in possible macro costs of €4.5 million in the third year. When substitution of lanadelumab is also considered, the budget impact in year 3 will be savings of € 1.6 million, as the price of lanadelumab is higher.

There is uncertainty about the number of patients eligible for treatment with routine prevention, growth in the number of patients over time, and the distribution of patients for the different routine prevention treatment options. The savings may be overestimated as the number of patients is likely to increase without lanadelumab substitution. The National Health Care Institute has therefore analysed two scenarios. In scenario 1, the number of patients eligible for routine prevention increases without substitution of lanadelumab, as berotralstat is more user-friendly than lanadelumab. In that case, there will be additional costs instead of savings. In scenario 2, the dosing frequency of lanadelumab is varied. If it is higher than expected, it will lead to greater savings.

Cost-effectiveness

As there is an equal value, an assessment of the cost-effectiveness of berotralstat is not required. However, it is not known whether the comparator products, namely C1 esterase inhibitors and lanadelumab, are cost-effective.

Should you need any further information, please do not hesitate to contact us. The assessment reports have been added as annexes (GVS report, budget impact analysis).

Yours sincerely,

National Health Care Institute
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Medicinal Products

M.J. Janssen
Chairperson of the Executive Board

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