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2025017092

National Health Care Institute
Research, Development and Medicinal Products
Medicinal Products Team

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Contact
Ms N. Stam
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Our reference
2025017092

Date 31 July 2025
Re: GVS advice omaveloxolone (Skyclarys®) for Friedreich ataxia

Dear Ms Jansen,

The National Health Care Institute advises you on the inclusion of omaveloxolone (Skyclarys®) for Friedreich ataxia in the Medicine Reimbursement System (GVS). This advice was prompted by your request in the letter dated January 2025 (CIBG-24-07729).

The National Health Care Institute advises you not to include omaveloxolone (Skyclarys®) for Friedreich ataxia in List 1B of the GVS, unless the net price can be significantly reduced after successful negotiations and an orphan drug arrangement is also drawn up.

Friedreich ataxia is a hereditary progressive disease that damages the nervous system. Due to a lack of the protein frataxin, nerve cells in the spinal cord, the brain and eventually the rest of the body die. Patients with Friedreich ataxia therefore have problems with coordination, balance and movement, fatigue and difficulty speaking. They also have a higher risk of heart disease and diabetes. The diagnosis is usually made before the patient is 25 years old. Most patients will need a wheelchair by the age of 30. Patients with Friedreich ataxia usually die between the age of 40 and 60 years. There are an estimated 160 patients in the Netherlands. The current standard of care consists of best supportive care, including rehabilitation and physiotherapy and symptomatic treatment of complications.

Registered indication
Omaveloxolone (Skyclarys®) is indicated for the treatment of Friedreich ataxia in adults and adolescents aged 16 years and older. The medicinal product is available in 50 mg capsules.

Claim by the marketing authorisation holder
Omaveloxolone (Skyclarys®) has an added value for the registered indication over standard treatment with best supportive care.

The marketing authorisation holder therefore requests inclusion in List 1B of the Health Insurance Regulation for the registered indication.

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Advisory report

The National Health Care Institute advises you not to include omaveloxolone (Skyclarys®) in the GVS, unless the net price can be reduced by 84% after successful price negotiations, and agreements for appropriate use are made. Omaveloxolone meets the legal criterion of 'established medical science and medical practice', but the cost-effectiveness is very unfavourable. Due to uncertainty about patient numbers, price-volume arrangements or a budget cap may be considered. The National Health Care Institute advises that the price negotiations should take into account the indication expansion to include younger children that may follow in the future.

If omaveloxolone is nevertheless included in the GVS after successful price negotiations, we advise you to place omaveloxolone (Skyclarys®) on List 2 of the GVS with the following additional conditions:

Condition omaveloxolone
Only for an insured person with Friedreich ataxia.

We have explained below how we reached this advisory report.

General

At your request, the National Health Care Institute assesses whether care should be part of the standard health insurance package from the perspective of the basic healthcare package paid from joint premiums.

The National Health Care Institute assesses on the basis of the four package criteria[1]: effectiveness[2], cost-effectiveness[3], necessity[4] and feasibility[5]. The Scientific Advisory Board (WAR) advises the National Health Care Institute on the (scientific) basis and the conclusion of the assessment. If there are risks regarding the accessibility and affordability, the assessment of the package criterion of effectiveness (established medical science and medical practice) will be placed in the wider social context of the four package criteria. The Insured Package Advisory Committee (hereinafter also "ACP") advises the Executive Board of the National Health Care Institute in this regard. This social weighting results in the package advice. Stakeholders are consulted during the process.

Substantive assessment

Assessment of interchangeability
Based on the criteria for interchangeability, the National Health Care Institute concluded that omaveloxolone is *not* interchangeable with other medicinal

[1] Real-world package management 4 (2023). National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl.

[2] Assessment of the established medical science and medical practice (2023). National Health Care Institute. Via www.zorginstituutnederland.nl.

[3] Healthcare cost-effectiveness report (2024) National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl.

[4] Necessity is related to both the medical need due to the severity of a disease for the patient (burden of disease) and the need to insure something. See the report on real-world package management 4 (2023).

[5] The package criterion of feasibility deals with whether it is feasible or sustainable to include a specific form of care in the basic healthcare package. It is therefore mainly a test of a number of implementation aspects such as the healthcare organisation, support, ethical and legal aspects, budget impact and so on. See the report on real-world package management 4 (2023).

products included in the GVS. As a result, omaveloxolone cannot be placed on List 1A. The National Health Care Institute has therefore assessed whether omaveloxolone can be included in List 1B.

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Therapeutic value
The National Health Care Institute, advised by the Scientific Advisory Board (WAR), concluded that omaveloxolone in Friedreich ataxia meets the established medical science and medical practice and has added value compared to standard treatment with best supportive care.

The randomised study (RCT) MOXIe part 2 has compared omaveloxolone with placebo in patients with Friedreich ataxia aged 16 years and older. The study shows that omaveloxolone has a small but clinically relevant effect on slowing down disease progression. In addition, omaveloxolone may have a clinically relevant effect on quality of life. It is still unknown how long the effects last and whether patients with Friedreich ataxia actually live longer with omaveloxolone. In addition, it is not clear which patients benefit most from the medicinal product and what the optimal duration of treatment is. The extension study shows that the effect of omaveloxolone on the delay in disease progression persists for 3 years, but patients continue to deteriorate. So the disease progression does not stop. The adverse reaction profile of omaveloxolone is acceptable. In particular, patients may experience gastrointestinal symptoms such as nausea, vomiting and diarrhoea.

Budget impact analysis
The National Health Care Institute estimates that 107 patients will be treated with omaveloxolone for the above indication in the third year after inclusion in the package. The total annual costs per patient are €245,572. This results in a budget impact of € 26 million in the third year after inclusion. There is no substitution of other medicinal products. There is some uncertainty about patient numbers.

In the future, there may be an expansion of the indication for omaveloxolone to include patients under 16 years of age. The National Health Care Institute expects this expansion to cover approximately 16 additional patients and to entail an increase in the macro cost of approximately €4 million.

Cost-effectiveness
In this case, the National Health Care Institute has chosen to write a brief note instead of a complete cost-effectiveness report. Indeed, a full pharmacoeconomic report does not appear to be appropriate, as omaveloxolone is clearly not a cost-effective intervention at the current asking price. The National Health Care Institute has concluded that the cost-effectiveness analysis of the marketing authorisation holder is of sufficient quality for decision-making. The cost-effectiveness estimate of the marketing authorisation holder is well above the reference value considered relevant for this disorder. The ICER is €1,937,363/QALY. A reference value of €80,000 would require an 84% reduction in the price of omaveloxolone to be cost-effective.

Social appraisal
The social appraisal shows that it is important for omaveloxolone to be available for the treatment of Friedreich ataxia, but only at a socially acceptable price. Because of the high cost of omaveloxolone, it is crucial that price negotiations

occur and that appropriate use agreements be made.

Appropriate use
Due to the high costs, uncertainty about which patients benefit most from omaveloxolone and the optimal treatment duration, the National Health Care Institute considers it necessary to make arrangements with the professional association to set up an indication commission and to agree on start and stop criteria, centralisation of treatment in centres of expertise, and the monitoring and recording of treatment results. This can promote appropriate use. The National Health Care Institute will contact the professional association, patient association and health insurers to provide a follow-up.

Should you need any further information, please do not hesitate to contact us. The assessment reports are attached (GVS report, pharmacotherapeutic report, budget impact analysis, pharmaco-economic note).

Yours sincerely,

M.J. Janssen
Chairperson of the Executive Board

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