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2024020167

Date 29 May 2024
Subject Package recommendation for the lock procedure medicinal product efgartigimod alfa (Vyvgart®)

Our reference
2024020167

Dear Ms Dijkstra,

The National Health Care Institute advises you about the evaluation of the medicinal product efgartigimod alfa (Vyvgart®) for the treatment of adult patients with refractory generalised myasthenia gravis (gMG) who are positive for the anti-acetylcholine receptor (AChR) antibody. This advice was prompted by the inclusion of efgartigimod alfa in the lock procedure for expensive medicinal products, thereby excluding efgartigimod alfa for all future indications.

Registered indication

Efgartigimod alfa is indicated as an addition to the standard therapy for treating adult patients with gMG who are positive for the anti-acetylcholine receptor (AChR) antibody.

Claim by the marketing authorisation holder

Efgartigimod alfa has added therapeutic value over the current standard treatment with repeated administration of normal human immunoglobulins and/or plasmapheresis in the treatment of patients with gMG in whom antibodies to the AChR are present and in whom symptomatic treatment and immunosuppressive treatment fail to control the disease.

Package advice

The National Health Care Institute advises you to include efgartigimod alfa (Vyvgart®) in the basic health care package for treating adult patients with refractory gMG who are positive for the anti-acetylcholine receptor (AChR) antibody, provided that price negotiations yield a net price that does not exceed that of eculizumab or ravulizumab.

The National Health Care Institute has established that efgartigimod alfa for adult patients with refractory gMG who are positive for the AChR antibody meets the legal criterion of 'established medical science and medical practice' and that there is equal therapeutic value compared to eculizumab. Based on the National Health Care Institute's earlier conclusion that eculizumab and ravulizumab have equal value, there is also equal therapeutic value to ravulizumab.

We have explained below how we reached this package advice.

General

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

The National Health Care Institute assesses on the basis of the four package criteria¹ of effectiveness², cost-effectiveness³, necessity⁴ and feasibility⁵. The Scientific Advisory Board (WAR) advises the National Health Care Institute on the scientific (and other) support and the conclusion of the assessment.

Effectiveness

Myasthenia gravis (MG) is a chronic autoimmune disease that affects neuromuscular transmission. This leads to fatigue and skeletal muscle weakness. In gMG, muscle groups in the head, neck, torso and/or extremities are affected. The involvement of the respiratory muscles may result in respiratory insufficiency. This is called a myasthenic crisis; it occurs in about 15% of patients with MG, especially in the early years of the disease. Although patients with MG generally have normal life expectancy, a myasthenic crisis is a life-threatening exacerbation of MG that can sometimes be fatal.

The medical management of MG consists of 3 stages:

1. Symptomatic treatment with the acetylcholinesterase inhibitors pyridostigmine, neostigmine or distigmine
2. Immunosuppressive treatment with corticosteroids, usually prednisolone.
3. Intravenous immunoglobulin (IVIg) or plasmapheresis in acute exacerbations of MG

However, a subset of patients respond suboptimally, even with chronic treatment with IVIg or plasmapheresis, or cannot tolerate the treatment. These patients are considered to be refractory cases.

In patients with refractory MG, the physician's association for gMG states that treatment should be considered with new drugs, such as the complement inhibitors eculizumab and ravulizumab, and inhibitors of the neonatal Fc receptor (FcRn), such as efgartigimod alfa. An indication committee has been set up to determine which patients are eligible for eculizumab or ravulizumab, which are now part of the health insurance package.

At the time of the assessment, ravulizumab was not yet covered in the insured care package and efgartigimod alfa was therefore only compared against

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

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

³ Cost-effectiveness report (2015). 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 type of care in the basic health care package. It is therefore mainly a test of a number of implementation aspects such as health care organisation, support, ethical and legal aspects, budget impact and so on. See the report on real-world package management 4 (2023).

eculizumab.

There is no direct comparative study between efgartigimod alfa and eculizumab; both treatments have been studied in randomised, double-blind, placebo-controlled, phase III trials.

Based on the results, the National Health Care Institute concludes that the effectiveness of eculizumab and efgartigimod alfa is likely to be similar. Efgartigimod alfa and eculizumab are also likely to have similar adverse effects. Based on the National Health Care Institute's earlier conclusion that eculizumab and ravulizumab have equal value, they conclude here that the therapeutic value will also be equal to ravulizumab.

Cost-effectiveness

Due to its equal therapeutic value, the National Health Care Institute has not assessed its cost-effectiveness.

Budget impact analysis

The National Health Care Institute estimates that 19 refractory gMG patients will be treated per year with efgartigimod alfa for this indication by year 3 after inclusion in the package. The total costs per patient per year are €345,510. This results in macro costs of €6.2 million in the third year. When substitution of eculizumab is taken into account, the budget impact in year 3 is €0.6 million.

Patients switching from efgartigimod alfa to eculizumab in the first two years, particularly from the marketing authorisation holders compassionate use programme, will lead to additional expenditure within the medical specialist care budget due to additional spending on eculizumab. However, these costs have not been included in this budget impact analysis because these medication costs do not derive from efgartigimod alfa.

The new complement inhibitor ravulizumab was not included in the budget impact analysis because it only became available in the Netherlands while this report was being written. A financial arrangement has been concluded by the Ministry of Health, Welfare and Sport. The cost of ravulizumab per patient per year is lower than for eculizumab or efgartigimod alfa (based on the PPP). Because of its equivalent value to eculizumab (and thus indirectly to ravulizumab), efgartigimod alfa should not be more expensive than ravulizumab.

Pricing agreements may also exist for eculizumab, which means that the savings for efgartigimod alfa may actually be lower than estimated in this BIA. Furthermore, the National Health Care Institute notes that biosimilars of eculizumab registered for the indication gMG may also enter the market in a few years, possibly triggering price falls.

Appropriate care

The physician's association for gMG has indicated that it will prescribe efgartigimod alfa through an indication committee, as is done for eculizumab and ravulizumab. Start and stop criteria will be applied that ensure that treatment will only take place if clinically relevant results are achieved.

Should you need any further information, please do not hesitate to contact us.

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The assessment reports have been added as annexes (pharmacotherapeutic report, budget impact analysis).

Yours sincerely,

Sjaak Wijma
Chair of the Executive Board

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