



> Return address PO Box 320, 1110 AH Diemen

To the Minister of Health, Welfare and Sport  
P.O. Box 20350  
2500 EJ THE HAGUE

2025003930

National Health Care Institute  
Care  
Medicinal Products

Willem Dudokhof 1  
1112 ZA Diemen  
P.O. Box 320  
1110 AH Diemen  
www.zorginstituutnederland.nl  
info@zinl.nl

T +31 (0)20 797 85 55

Contact  
E. De Groot  
warcg@zinl.nl

Date 24 February 2025  
Re: GVS advice rozanolixizumab (Rystiggo®) for myasthenia gravis

Our reference  
2025003930

Dear Ms Agema,

The National Health Care Institute advises you on the inclusion of rozanolixizumab (Rystiggo®) for the treatment of refractory generalised myasthenia gravis (gMG) in the Medicine Reimbursement System (hereinafter "GVS"). The reason we are issuing this advice is your request in the letter of 30 September 2024 CIBG-24-07398.

In patients with myasthenia gravis (MG), the immune system targets its own body. The immune system damages the components that normally transmit stimuli from the nerve to the muscle.

In most patients with MG, this affects the acetylcholine receptor (AChR). In some patients (3-5%), muscle-specific kinase (MuSK) is affected.

In both types of patients, muscle weakness develops in different ways, depending on the affected muscles. Sudden temporary worsening of the disease may also occur. The characteristics and severity of MG vary widely from patient to patient. Generalised MG (gMG) affects muscles in the head, neck, torso or extremities. Although patients with gMG have a normal life expectancy, 15% of patients may experience life-threatening respiratory failure, a so-called myasthenic crisis. Approximately 2500 patients in the Netherlands suffer from MG. In 2019, 565 patients with gMG were registered in the Dutch myasthenia registry.

The standard treatment of MG consists of 3 steps (acetylcholinesterase inhibitors, immunosuppressive treatment and intravenous immunoglobulin (IVIg) or plasmapheresis/plasma exchange in acute MG exacerbations). However, some patients need more than the standard treatment. These patients are called refractory and can currently be treated with eculizumab, ravulizumab, efgartigimod alfa and zilucoplan. For patients with refractory gMG who are MuSK antibody positive, no targeted treatment is currently available.

#### Registered indication

Rozanolixizumab (Rystiggo®) is indicated as an adjuvant to standard therapy for the treatment of generalised myasthenia gravis (gMG) in adult patients who have been tested positive for antibodies to the acetylcholine receptor (AChR) or to the muscle-specific receptor tyrosine kinase (MuSK).

Rozanolixizumab is available as a solution for subcutaneous injection at a

concentration of 120 mg/ml, in vials of 2, 3, 4, 5 and 6 ml. Rozanolixizumab should be administered weekly in cycles of 6 weeks at a weight-dependent dose.

National Health Care Institute  
Care  
Medicinal Products

#### Claim by the marketing authorisation holder

The marketing authorisation holder requests inclusion in List 1B of the Health Insurance Regulation for the treatment of adult patients with refractory gMG who test positive for antibodies to AChR and MuSK. The MAH claims an equal value in relation to eculizumab and ravulizumab.

Date  
24 February 2025  
Our reference  
2025003930

#### **Advice**

The National Health Care Institute recommends that rozanolixizumab (Rystiggo®) for treating adult patients with refractory generalised myasthenia gravis (gMG) who test positive for antibodies to AChR or MuSK be included in List 1A of the GVS in a newly formed cluster with zilucoplan (Zilbrysq®).

The inclusion of rozanolixizumab should not lead to additional costs compared to the costs associated with treatment with zilucoplan due to its interchangeability with zilucoplan.

The standard dose for rozanolixizumab is set at 80 mg daily and 23 mg daily for zilucoplan.

In addition, we advise you to place rozanolixizumab (Rystiggo®) on List 2 of the GVS with the same further condition as zilucoplan:  
Exclusively for an insured person for whom the medicinal product has been prescribed by an academic centre after approval by the Generalised Myasthenia Gravis (gMG) indication committee.

We explain the preparation of this advice below.

#### Outcome of the substantive assessment *Assessment of interchangeability*

Based on the criteria for interchangeability, the National Health Care Institute has concluded that rozanolixizumab is interchangeable with zilucoplan, which is included in List 1B of the Health Insurance Regulation.

#### *Therapeutic value*

The National Health Care Institute has concluded that rozanolixizumab has an equivalent value with ravulizumab and eculizumab in adult patients with refractory gMG who test positive for antibodies to AChR, and thus complies with the established medical science and medical practice. Rozanolixizumab also complies with the established medical science and medical practice for treating adult patients with refractory generalised myasthenia gravis (gMG) who test positive for MuSK antibodies.

The National Health Care Institute recently assessed zilucoplan and efgartigimod alfa for the present indication. For both medicinal products, an equal value with eculizumab and ravulizumab was concluded. A similar approach is now being used for rozanolixizumab, for which the interchangeability with zilucoplan is also assessed, which is already included in the GVS.

The effectiveness and safety of rozanolixizumab has only been studied compared to placebo. Zilucoplan, eculizumab and ravulizumab have also only been studied

compared to placebo in randomised trials. All medicinal products result in a reduction in the severity of the disease.

Rozanolixizumab is the only product also indicated for patients with MuSK antibodies. Subgroup analyses show similar effectiveness in these patients compared to the entire study population.

#### *Budget impact analysis*

Rozanolixizumab is interchangeable with zilucoplan, and both medicinal products can, therefore, be clustered. For an estimate of the budget impact for refractory gMG patients with antibodies to AChR, the National Health Care Institute refers to the budget impact analysis for zilucoplan. Since rozanolixizumab has an indication for AChR-positive patients as well as an indication for MuSK-positive patients, a budget impact note is attached specifically for this latter group. For patients with MuSK-antibodies, the National Health Care Institute estimates that 8 refractory gMG patients per year will be treated with rozanolixizumab in year 3 after inclusion in the package. The total costs per patient per year are €310,849. This results in a budget impact of the MuSK-positive patients of €2.5 million in the third year. There is uncertainty about the number of cycles administered per year, as the treatment depends on the response. If in practice patients respond less well than in the clinical trial, the costs may be higher.

#### *Cost-effectiveness*

As there is an equal value, an assessment of the cost-effectiveness of rozanolixizumab is not required. However, it is not known whether the comparator products, namely zilucoplan, ravulizumab and eculizumab, are cost-effective.

#### *Reimbursement framework*

Rozanolixizumab was, in contrast to eculizumab, ravulizumab and efgartigimod alfa, identified as an extramural medicine based on the demarcation letter<sup>1</sup>. Based on your Ministry's (Ministry of Health, Welfare and Sport) current policy, it is not possible to deviate from this at present. The National Health Care Institute notes that it may have adverse effects if part of the medicinal products are claimed for this indication through a different reimbursement framework. This could result in an uneven playing field with a potentially financially driven preference for one of the products, which would not necessarily result in lower costs for the public. It is possible that the costs of inpatient medicines may be lower through price arrangements than the costs of extramural medicines (via the GVS).

#### *Appropriate Care*

An indication committee has been set up to assess which refractory gMG patients in the Netherlands are eligible for eculizumab or ravulizumab. The National Health Care Institute proposes to include rozanolixizumab in the existing orphan drug arrangement.

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

Yours sincerely,

---

<sup>1</sup> Ministry of Health, Welfare and Sport (2014) Afbakening aanspraak Farmaceutische Zorg en aanspraak Geneeskundige Zorg met betrekking tot geneesmiddelen (Demarcation of entitlement to Pharmaceutical Care and entitlement to Medical Care with regard to medicinal products). (Reference number: 183496-115412-GMT)

M.J. Janssen  
Chairperson of the Executive Board

National Health Care Institute  
Care  
Medicinal Products

Date  
24 February 2025

Our reference  
2025003930