



> Return address PO Box 320, 1110 AH Diemen

To the Minister of Health, Welfare and Sport  
P.O. Box 20350  
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2025025885

Date 30 October 2025  
Re: Package advice lock procedure medicinal product ravulizumab  
(Ultomiris®) for neuromyelitis optica spectrum disorder (NMOSD)

Dear Mr Bruijn,

The National Health Care Institute advises you on the assessment of ravulizumab (Ultomiris®) for neuromyelitis optica spectrum disorder (NMOSD) This advice was prompted by the placement of ravulizumab in the package lock for expensive medicinal products.

The National Health Care Institute advises you to include ravulizumab for the treatment of adult patients with NMOSD who are anti-aquaporin 4 (AQP4) antibody-positive in the basic healthcare package.

NMOSD is a rare disease of the nervous system that mainly affects the optic nerves and the spinal cord. NMOSD is an autoimmune disease. This means that the immune system is attacking the patient's own body. This causes inflammation, especially in the optic nerves and spinal cord. People experience sudden loss of vision, loss of strength or paralysis in arms or legs. They may also suffer from pain or a burning sensation in the back or arms or legs, and problems with urination or bowel movements. There are several forms of the disease. Patients who are 'AQP4 positive' often have a more severe disease progression with sudden flare-ups. These are also called relapses, where the body again attacks the nervous system. These attacks can lead to serious symptoms if left untreated. An attack can damage the nerves. In the Netherlands, patients are initially treated with the medicinal product rituximab, which suppresses the immune system. If this no longer works sufficiently, people may be eligible for other immune suppressants, such as eculizumab, inebilizumab and satralizumab.

Around 200 people in the Netherlands have NMOSD. 17 people are diagnosed with NMOSD every year. Of these, 80% are AQP4 positive. Every year, approximately 5 AQP4-positive patients have an inadequate response to rituximab.

#### Licensed indication

Ravulizumab (Ultomiris®) is indicated for the treatment of adult patients with NMOSD who are anti-aquaporin 4 (AQP4) antibody-positive.

In addition, ravulizumab (Ultomiris®) is also registered for certain patients with paroxysmal nocturnal haemoglobinuria (PNH), atypical haemolytic uraemic syndrome (aHUS) and generalised myasthenia gravis (gMG). The National Health

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#### **Our reference**

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Care Institute has already assessed ravulizumab for PNH and gMG and these indications are already being reimbursed. The National Health Care Institute is currently also evaluating treatment of aHUS with ravulizumab.

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#### Claim by the marketing authorisation holder

Ravulizumab (Ultomiris®) has an equal value to eculizumab for patients with NMOSD who are AQP4-IgG positive *and who can no longer be treated with rituximab*.

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#### **Package advice**

The National Health Care Institute advises you to include ravulizumab (Ultomiris®) for the treatment of adult patients with NMOSD who are anti-aquaporin 4 (AQP4) antibody-positive and can no longer be treated with rituximab in the basic healthcare package, provided that the inclusion in the package does not result in additional costs.

The National Health Care Institute has established that ravulizumab for the claimed indication meets the legal criterion of 'established medical science and medical practice' and that there is an equal value to the standard treatment with eculizumab, satralizumab and inebilizumab.

We explain the preparation of this package advice below.

#### 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<sup>1</sup>: effectiveness<sup>2</sup>cost-effectiveness<sup>3</sup>, necessity<sup>4</sup> and feasibility<sup>5</sup>. Stakeholders are consulted during the process.

#### Comprehensive weighting of package criteria

##### *Effectiveness*

##### *Established medical science and medical practice*

There are no randomised studies available in which ravulizumab is directly compared to eculizumab, inebilizumab and satralizumab. Ravulizumab has therefore been indirectly compared to these treatments. Naïve comparisons and a network meta-analysis (NMA) were used for this.

Clinically relevant relapse effects are observed for all four medicinal products. The risk of a relapse and the annual relapse rate (ARR) decrease. In addition, the time

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<sup>1</sup> Real-world package management 4 (2023). National Health Care Institute, Diemen. Via [www.zorginstituutnederland.nl](http://www.zorginstituutnederland.nl).

<sup>2</sup> Assessment of the established medical science and medical practice (2023). National Health Care Institute. Via [www.zorginstituutnederland.nl](http://www.zorginstituutnederland.nl).

<sup>3</sup> Healthcare cost-effectiveness report (2024) National Health Care Institute, Diemen. Via [www.zorginstituutnederland.nl](http://www.zorginstituutnederland.nl).

<sup>4</sup> 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).

<sup>5</sup> 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, the support base, ethical and legal aspects, budget impact, etc. See the report on real-world package management 4 (2023).

to first relapse increases, compared to placebo. There also seems to be a small positive effect on the quality of life and the degree of disability. There are no obvious differences in the occurrence of serious side effects. In the studies, patients previously treated with rituximab appear to have similar outcomes to those who have not been previously treated.

Ravulizumab is a modified variant of eculizumab, extending the half-life in the body. This allows for a lower administration frequency. As a result, ravulizumab may be more user-friendly than eculizumab.

The National Health Care Institute concludes that ravulizumab for adult patients with NMOSD who are anti-aquaporin 4 (AQP4) antibody-positive and can no longer be treated with rituximab is equivalent to standard treatment with eculizumab, inebilizumab and satralizumab.

#### *Cost-effectiveness*

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

The National Health Care Institute also did not perform a cost-effectiveness analysis of eculizumab, satralizumab or inebilizumab for this indication; it is therefore unknown what a cost-effective price would be in the Netherlands.

#### Budget impact analysis

The National Health Care Institute estimates that 12 patients per year will be treated with ravulizumab for the above indication in year 3 after inclusion in the package. The total costs per patient per year are €267,768. This results in possible macro costs of €2.9 million in the third year. When substitution of eculizumab, satralizumab or inebilizumab is also taken into account, the budget impact in year 3 is €520,713. This is based on the list prices. In reality, prices may be lower. In 2017, the National Health Care Institute recommended a 90% discount for eculizumab for the indication PNH.

Based on the equal value conclusion, inclusion of ravulizumab in the basic healthcare package should not result in additional costs compared to the current actual costs of treatment with eculizumab, inebilizumab and satralizumab for NMOSD. It should be taken into account that the introduction of future eculizumab biosimilars may lead to a decrease in the price of eculizumab. This price decrease should also have an impact on the price of ravulizumab, so that ravulizumab will continue to cost no more than eculizumab.

Indication expansions lead to a larger sales market and more volume. Therefore, the negotiated price of ravulizumab for previously negotiated indications should be the starting point, as indication expansions should not be accompanied by price increases.

#### **Appropriate care**

In 2020, the joint healthcare insurers prepared an orphan drug arrangement for eculizumab, satralizumab, tocilizumab and inebilizumab for the rare condition NMOSD. The National Health Care Institute considers it important that ravulizumab is added to this.

Should you need any further information, please do not hesitate to contact us. The assessment reports have been added as annexes (pharmacotherapeutic

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report and budget impact analysis).

Yours sincerely,

M.J. Janssen  
*Chairperson of the Executive Board*

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