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National Health Care Institute
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2022035402

Our reference
2022035402

Date 16 September 2022
Subject Package advice lock procedure medicinal product pegcetacoplan (Aspaveli®)

Dear Mr Kuipers,

The National Health Care Institute advises you on pegcetacoplan (Aspaveli®) for the treatment of adult patients with paroxysmal nocturnal haemoglobinuria (PNH) who are anaemic after treatment with a C5 inhibitor for at least 3 months. The reason for this advisory report was the placement of the above-mentioned medicinal product in what is known as the 'lock procedure' for expensive medicinal products.

Following pegcetacoplan's placement in the lock procedure, the National Health Care Institute has assessed the reimbursement for this medicinal product. The marketing authorisation holder has submitted a dossier, in the context of the package management of specialist medicinal products. During the assessment, the National Health Care Institute and the Ministry of Health, Welfare and Sport jointly came to the conclusion that, on the basis of the demarcation letter[1], pegcetacoplan should be designated as an outpatient medicine. The medicinal product is a subcutaneous injection that the patient can administer at home. However, the National Health Care Institute takes the view that, in the case of pegcetacoplan, inpatient funding is both logical and appropriate. To date, every medicinal product that has been made available for the treatment of PNH has been funded intramurally. The funding of all medicinal products via the same route creates a level playing field, and encourages appropriateness more effectively. The National Health Care Institute understands that, at the present time, the demarcation letter must be leading. However, it advises the Ministry of Health, Welfare and Sport to give broader consideration to the demarcation policy.

The National Health Care Institute has concluded that pegcetacoplan meets the established medical science and medical practice for the indication above. The National Health Care Institute has determined that pegcetacoplan has added value compared to eculizumab and ravulizumab.
However, the use of pegcetacoplan is associated with additional costs. The

[1] 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

National Health Care Institute
Care
Medicinal Products

Date
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Our reference
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National Health Care Institute is unable to determine the exact amount of these additional costs because the actual price of eculizumab is not known.
We advise you to include pegcetacoplan in the package, provided that a price reduction is achieved. In 2017, the National Health Care Institute recommended a 90% discount for eculizumab. In 2021, the National Health Care Institute advised to negotiate a price for ravulizumab that should in any case not be higher than the negotiated price of eculizumab.
For pegcetacoplan, the National Health Care Institute recommends an 85% price reduction, based on a 90% reduction for eculizumab. The negotiations should take into account the introduction of biosimilars for eculizumab, possible indication extension in the future and the possible arrival of competitive products. In addition, the PNH orphan drug arrangement will be expanded with pegcetacoplan.

In this letter, I explain our findings and final conclusion.

General

At your request, the National Health Care Institute assesses whether new care should be part of the basic health insurance package from the perspective of the basic health care package paid from joint premiums. The National Health Care Institute has assessed pegcetacoplan on the basis of the four package criteria[2] of effectiveness[3], cost-effectiveness[4], necessity and feasibility. We consider these both in the scientific sense and in terms of public support. We also review the aspects of efficiency and transparency. The National Health Care Institute is advised in its package reviews by two independent committees:

- the Scientific Advisory Board (WAR) for the review of data according to the established medical science and medical practice, and to determine the cost-effectiveness; and
- the Insured Package Advisory Committee (ACP) for the social deliberations.

We also consulted stakeholders during the assessment process.

Comprehensive weighting of package criteria

Established medical science and medical practice

The efficacy and safety of pegcetacoplan have been investigated in a phase III, randomized, actively controlled, open-label study (PEGASUS) in adult patients with PNH with haemoglobin values of <10.5 g/dl (corresponding to <6.5 mmol/L) after treatment with eculizumab for at least 3 months.
Treatment with pegcetacoplan resulted in clinically relevant improvement of haemoglobin values compared to eculizumab; 34.1% of patients in the pegcetacoplan arm reached normalisation of haemoglobin values, while none of the patients in the treatment arm with eculizumab reached normalisation. More patients treated with pegcetacoplan achieved lactate dehydrogenase (LDH) normalisation compared to eculizumab (71% vs 15%). A large number of patients in the eculizumab arm received a transfusion (85%) compared to patients treated with pegcetacoplan (15%).
The National Health Care Institute concludes that pegcetacoplan in the treatment

[2] *Real-world package management 3* (2013). National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl.

[3] *Established medical science and medical practice assessment: updated version* (2015). National Health Care Institute,
Diemen. Via www.zorginstituutnederland.nl .

[4] *Cost-effectiveness report* (2015). National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl .

National Health Care Institute
Care
Medicinal Products

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of adult patients with paroxysmal nocturnal haemoglobinuria who, after treatment for at least 3 months with a C5 inhibitor, are anaemic with a haemoglobin value <6.5 mmol/L has an added value compared to eculizumab and ravulizumab and therefore meets the established medical science and medical practice.

Budget impact
The costs per patient per year for pegcetacoplan (based on the list price) are €346,898 in the first year, €316,050 in subsequent years. In the third year, taking into account a market penetration of 100%, a total of 24 PNH patients who would otherwise continue to use eculizumab, are expected to be eligible for treatment with pegcetacoplan. The cost savings amount to €0.6 million in the third year (based on the list price).

Cost-effectiveness
The cost-effectiveness model is of sufficient quality. The marketing authorisation holder reports a dominant ICER (-€247,126) compared to eculizumab. The National Health Care Institute wishes to emphasize that the list price of eculizumab has been used. In the past, it has been advised not to reimburse eculizumab unless a price reduction of 90% could be achieved. The ministry negotiated the price of eculizumab. The outcome of these negotiations is confidential. When the price reduction of 90% for eculizumab is applied in the model, the ICER is no longer dominant, but €1,668,496. A price reduction of 85% on average is needed for the treatment to be considered cost-effective (based on a reference value of €20,000). If the model (as an example) applies a price reduction of 35%[5] for eculizumab, the ICER is €497,828. In that case, a price reduction of 25% on average is needed to consider this a cost-effective treatment.

Orphan drugs arrangement
To monitor and track the appropriate use of pegcetacoplan, the existing orphan drugs arrangement for PNH, with eculizumab and ravulizumab, will be extended to include pegcetacoplan.

Final conclusion
The National Health Care Institute has concluded that pegcetacoplan meets the established medical science and medical practice for the indication above. The National Health Care Institute has determined that pegcetacoplan has added value compared to eculizumab and ravulizumab.
However, the use of pegcetacoplan is associated with additional costs. The National Health Care Institute is unable to determine the exact amount of these additional costs because the actual price of eculizumab is not known.
We advise you to include pegcetacoplan in the package, provided that a price reduction is achieved. In 2017, the National Health Care Institute recommended a 90% discount for eculizumab. In 2021, the National Health Care Institute advised to negotiate a price for ravulizumab that should in any case not be higher than the negotiated price of eculizumab.
For pegcetacoplan, the National Health Care Institute recommends an 85% price reduction, based on a 90% reduction for eculizumab. The negotiations should take into account the introduction of biosimilars for eculizumab, possible indication extension in the future and the possible arrival of competitive products. In addition, the PNH orphan drug arrangement will be expanded with pegcetacoplan.

[5] based on the average price discount achieved by the ministry in 2018, the year in which a financial arrangement was agreed for eculizumab

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If the application of pegcetacoplan is included in the package after successful price negotiations, the National Health Care Institute recommends the following reimbursement condition:

Condition for pegcetacoplan
Only for an insured person with paroxysmal overnight haemoglobinuria who is anaemic after treatment with a C5 inhibitor for at least 3 months, with a haemoglobin value of <6.5 mmol/L.

Yours sincerely,

Sjaak Wijma
Chairperson of the Executive Board