Zorginstituut Nederland

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To the Minister of Health, Welfare and Sport
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2025000492

Date 18 March 2025
Re: GVS advice iptacopan (Fabhalta®) for paroxysmal nocturnal haemoglobinuria (PNH)

National Health Care Institute
Care
Medicinal Products

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Our reference
2025000492

Dear Ms Agema,

This is a corrected version of the letter already sent on 25 February 2025. In the paragraph 'Budget impact analysis', the number of patients has been adjusted from 6 to 9. This change has also been made in the attached PT report and the budget impact analysis.

The National Health Care Institute advises you on the inclusion in the Medicine Reimbursement System (GVS) of iptacopan (Fabhalta®) for patients with paroxysmal nocturnal haemoglobinuria (PNH) who remain anaemic despite treatment with a C5 inhibitor. This advice was prompted by your request in the letter of 4 November 2024 (CIBG-24-07512).

PNH is a non-hereditary, rare bone marrow disease. Approximately 125 patients have been diagnosed with this disease in the Netherlands. Patients with PNH suffer from severe anaemia. This anaemia is due to the increased breakdown of red blood cells, infections that cause the breakdown of white blood cells, and thrombosis. Untreated PNH patients have a reduced quality of life and reduced life expectancy.

Registered indication
Iptacopan (Fabhalta®) is indicated as monotherapy for the treatment of adult PNH patients with paroxysmal nocturnal haemoglobinuria who have haemolytic anaemia.

Claim by the marketing authorisation holder
Iptacopan has at least the same value as pegcetacoplan and added value over continued treatment with eculizumab or ravulizumab in PNH patients who remain anaemic despite treatment with a C5 inhibitor. For the purpose of the assessment, only the equal value claim is relevant in relation to the comparable place with pegcetacoplan in the treatment of PNH.

Reimbursement is requested for part of the registered indication, namely for patients with PNH who remain anaemic after treatment with a C5 inhibitor (eculizumab or ravulizumab). The marketing authorisation holder therefore requests inclusion in List 1B of the Health Insurance Regulation with the same List

2 condition as for pegcetacoplan. Iptacopan is available in 200 mg capsules The daily dose is 400 mg.

Advice
The National Health Care Institute recommends that iptacopan (Fabhalta®) for patients with PNH who remain anaemic after treatment with a C5 inhibitor should be included in List 1B of the GVS, with the List 2 condition described below.

Condition iptacopan
Only for an insured person with paroxysmal nocturnal haemoglobinuria who, after at least 3 months of treatment with a C5 inhibitor remains anaemic with a haemoglobin level of <6.5 mmol/L , or in case of C5 inhibitor intolerance.

We recommend that the above adjustment of the List 2 condition in italics also be made for the List 2 condition of pegcetacoplan.

We explain the preparation of this advice below.

Substantive assessment

Assessment of interchangeability
Based on the criteria for interchangeability, the National Health Care Institute concluded that iptacopan is not interchangeable with other medicinal products included in the GVS. For the above indication, only pegcetacoplan administered subcutaneously is included in the GVS. On this basis, iptacopan cannot be placed on List 1A. For that reason, the National Health Care Institute has assessed the possibility of including iptacopan in List 1B.

Therapeutic value
Recently, the National Health Care Institute assessed pegcetacoplan for PNH[1]. At the time, it was concluded that pegcetacoplan, based on a randomised study compared to C5 inhibitors, meets the established medical science and medical practice and has added value compared to ravulizumab and eculizumab. A similar study was performed for iptacopan. A direct comparative study of pegcetacoplan vs. iptacopan is not available, which is why an indirect comparison has been made. This shows that the beneficial effects of iptacopan are comparable to those of pegcetacoplan: iptacopan leads in a similar degree to a clinically relevant decrease in transfusion dependence, change in haemoglobin and improvement of quality of life.

The pegcetacoplan and iptacopan studies have different inclusion criteria, namely inclusion of patients treated with a C5 inhibitor for at least 3 months and at least 6 months, respectively. Since pegcetacoplan and iptacopan are both C3 inhibitors and have similar beneficial effects and the professional association sees a similar secondary healthcare position for both products, the National Health Care Institute recommends an equal List 2 condition for both products, i.e. after 3 months of treatment with a C5 inhibitor.
In addition, based on information from the professional association, the National Health Care Institute also recommends that patients who are C5 inhibitor intolerant should be eligible for iptacopan and pegcetacoplan.

[1] Package advice medicinal product pegcetacoplan (Aspaveli®) for the treatment of paroxysmal nocturnal haemoglobinuria (PNH) | Advice | National Health Care Institute

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Met opmerkingen [AVB1]: Opmerking vertaler: although 'onafhankelijkheid' means 'independence', I have changed the translation to 'dependence' because of 'afname'. I think 'afname' should actually have been 'toename' in which case the translation would have been '...clinically relevant increase in transfusion independence...'.

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The National Health Care Institute, advised by the Scientific Advisory Board (WAR), has concluded that iptacopan has a therapeutic equivalent value to standard treatment/usual treatment with pegcetacoplan for said indication.

Budget impact analysis
The National Health Care Institute estimates that 9 patients per year are treated with iptacopan for the above indication in year 3 after inclusion in the insured package. The total costs per patient per year are €313,900. The macro costs of iptacopan are €2,825,100 per year in the first to third year after inclusion in the package. Taking into account the substitution of pegcetacoplan, the budget impact is -€230,180 in the first year and -€40,100 in years 2 and 3 after inclusion in the insured package (based on list prices). The inclusion of iptacopan in the insured package therefore does not lead to additional costs compared to pegcetacoplan.

Cost-effectiveness:
In its recommendation for pegcetacoplan of September 2022, the National Health Care Institute recommended a price reduction to achieve a cost-effective treatment. On the basis of this price reduction and the conclusion of equal value mentioned above, the price of iptacopan should be determined so that it can also be used cost-effectively.

In addition, The National Health Care Institute has been informed that, in practice, pegcetacoplan and C5 inhibitors are sometimes combined. The cost-effectiveness of this has not been investigated. The National Health Care Institute recommends monitoring the combined use of C3 and C5 inhibitors for the present indication to determine whether a cost-effectiveness analysis should be considered.

Appropriate care
To ensure the appropriate use of iptacopan, the existing orphan drug arrangement or the current guideline for the treatment of PNH will need to be extended to include iptacopan. In addition, The National Health Care Institute also recommends that the combined use of C5 and C3 inhibitors for PNH be registered.

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

Yours sincerely,

M.J. Janssen
Chairperson of the Executive Board