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Our reference
2025021239

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Date 10 September 2025
Subject GVS advisory report on danicopan (Voydeya®) for paroxysmal nocturnal haemoglobinuria

Dear Mr Bruijn,

This is a rectification to the letter sent to your predecessor on 8 May 2025 (reference 2024011457). The GVS report has also been amended.

The National Health Care Institute is hereby advising you about including danicopan (Voydeya®) as an adjunct to ravulizumab or eculizumab for treating paroxysmal nocturnal haemoglobinuria (PNH) in the Medicine Reimbursement System (hereinafter also "GVS"). The reason we are issuing this advisory report is the request you made in the letter of 17 February 2025 (CIBG-25-07864). The National Health Care Institute recommends that danicopan (Voydeya®) should be included on Annex 1B of the GVS as an adjunct to ravulizumab or eculizumab for PNH patients who have residual haemolytic anaemia as the result of clinically significant extravascular haemolysis (EVH).

PNH is a rare, non-hereditary bone marrow condition. There are 125 patients known to have 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 patients have a reduced quality of life and a lowered life expectancy. In the Netherlands, patients are treated primarily with a C5 inhibitor (eculizumab or ravulizumab). If patients continue to suffer anaemia despite treatment with a C5 inhibitor, pegcetacoplan is used.

Licensed indication
Danicopan (Voydeya®) is indicated as an adjunct to ravulizumab or eculizumab for treating adult patients with paroxysmal nocturnal haemoglobinuria (PNH) who have residual haemolytic anaemia. It is available as 50 mg and 100 mg film-coated tablets. The recommended dose is 150 mg three times daily.

Claim by the marketing authorisation holder
Danicopan (Voydeya®) as an adjunct to ravulizumab or eculizumab has added value over pegcetacoplan in PNH patients who have residual haemolytic anaemia caused by clinically significant extravascular haemolysis (EVH).

The marketing authorisation holder is therefore requesting inclusion on Annex 1B

of the Healthcare Insurance Regulations

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Advisory report
The National Health Care Institute recommends that danicopan (Voydeya®) should be included on Annex 1B of the GVS as an adjunct to ravulizumab or eculizumab for PNH patients who have residual haemolytic anaemia, with the Annex 2 conditions stated below. Because the National Health Care Institute has concluded that danicopan combined with a C5 inhibitor (eculizumab or ravulizumab) has a therapeutic effect comparable to pegcetacoplan (monotherapy), the actual costs of danicopan combined with a C5 inhibitor (eculizumab or ravulizumab) may not exceed the actual costs of pegcetacoplan (monotherapy).

Conditions for danicopan
Only for an insured person with paroxysmal nocturnal haemoglobinuria who, after treatment for at least 3 months with a C5 inhibitor, is anaemic with a haemoglobin value of <6.5 mmol/l.

We have explained below how we reached this advisory report.

Substantive assessment

Assessment of interchangeability
Danicopan cannot be clustered with pegcetacoplan because of differences in the method of administration. The National Health Care Institute recently advised you[1] to include another proximal complement inhibitor, iptacopan, in the GVS and place it in Annex 1B. The method of administration is the same for iptacopan as for danicopan. When assessing the criteria of interchangeability, danicopan was therefore compared against the medicinal product iptacopan. The indications applicable to danicopan and iptacopan are not the same. Danicopan is thus not interchangeable with any other product in the GVS. The National Health Care Institute then assessed whether danicopan can be included in Annex 1B.

Therapeutic value
Recently, the National Health Care Institute assessed pegcetacoplan for PNH[2]. The conclusion drawn, based on a randomised study comparing it against C5 inhibitors, is that pegcetacoplan monotherapy for treating adult patients with PNH who, after treatment for at least 3 months with a C5 inhibitor, are anaemic with a haemoglobin value of <6.5 mmol/L has added value compared to the C5 inhibitors eculizumab or ravulizumab and therefore meets the criterion of established medical science and medical practice. A study was also conducted for danicopan as an adjunct to eculizumab or ravulizumab in patients who remained anaemic after at least 3 months of treatment with a C5 inhibitor. No direct controlled study comparing pegcetacoplan to danicopan as an adjunct to eculizumab or ravulizumab is available; an indirect naive comparison was therefore made. This showed that the beneficial effects of danicopan as an adjunct to eculizumab or ravulizumab are similar to those of pegcetacoplan monotherapy: danicopan as an adjunct to eculizumab or ravulizumab yields a similar clinically relevant decrease

[1] https://www.zorginstituutnederland.nl/publicaties/adviezen/2025/03/18/gvs-advies-iptacopan-fabhalta-bij-pnh

[2] https://www.zorginstituutnederland.nl/publicaties/adviezen/2022/09/16/pakketadvies-sluisgeneesmiddel-pegcetacoplan-aspaveli

in transfusion independence, change in haemoglobin level and improvement in quality of life.

The National Health Care Institute, advised by the Scientific Advisory Board (WAR), has concluded that danicopan as an adjunct to a C5 inhibitor has a therapeutic effect comparable to treatment with pegcetacoplan for adult PNH patients (aged ≥18) with residual anaemic haemolysis as a result of csEVH (clinically significant extravascular haemolysis). The National Health Care Institute recommends similar Annex 2 conditions for both medicinal products, namely after at least 3 months of treatment with a C5 inhibitor.

Budget impact analysis
The National Health Care Institute estimates that 8 patients per year will be treated with danicopan for the stated indication in year 3 after inclusion in the package. The costs per patient per year are €54,449 for danicopan and €369,269 for danicopan plus a C5 inhibitor. In year 3, the macro cost impact of danicopan alone is €408,367 and the macro cost impact of danicopan plus C5 inhibitor is €2,769,517. There will be substitution of pegcetacoplan (plus the loading dose of the C5 inhibitor), for which the costs per patient per year are €339,810. As a result, the budgetary impact of including danicopan plus a C5 inhibitor comes to €375,382 in year 3. Because the National Health Care Institute has concluded that danicopan as an adjunct to eculizumab or ravulizumab has a therapeutic effect comparable to pegcetacoplan (monotherapy), the actual costs of danicopan combined with eculizumab or ravulizumab may not exceed the actual costs of pegcetacoplan (monotherapy).

Appropriate care
The range of PNH drugs has expanded in just a short time. To ensure appropriate use of danicopan as an adjuvant to eculizumab or ravulizumab, the existing orphan drug arrangements or the current guideline for PNH treatment will be extended to include danicopan and other drugs. In addition, the National Health Care Institute also recommends licensing the combined use of C5 inhibitors and proximal complement inhibitors for PNH. The National Health Care Institute is in discussions with the occupational group.

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

Yours sincerely,

M.J. Janssen
Chair of the Executive Board

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