National Health Care Institute

> Return address PO Box 320, 1110 AH Diemen

Minister of Medical Care
PO Box 20350
2500 EJ THE HAGUE

2024021702

National Health Care Institute
Care
Medicinal Products

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

T +31 (0)20 797 85 55

Contact
K. Watson
warcg@zinl.nl

Our reference
2024021702

Date 11 June 2024
Re: Package advice glofitamab (Columvi®)

Dear Ms Dijkstra,

This message contains the package advice for glofitamab (Columvi®) for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy. The reason for this advice was the placement of glofitamab in the lock procedure for expensive medicinal products.

Registered indication
Glofitamab is indicated as monotherapy for the treatment of adult patients with R/R DLBCL after two or more lines of systemic therapy.

Claim by the marketing authorisation holder
For the treatment of patients with R/R DLBCL who have previously received at least two systemic therapies and have been pre-treated with a single dose of obinutuzumab, glofitamab has a therapeutic value equivalent to treatment with polatuzumab vedotin in combination with bendamustine and rituximab (Pola-BR).

Package advice

The National Health Care Institute advises you to not include glofitamab in the health insurance package for the treatment of adult patients with R/R DLBCL who have previously received at least two systemic therapies. The development of this package advice is explained 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[1], effectiveness[2], cost-

[1] Real-world package management 4 (2023). National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl.
[2] Assessment of the established medical science and medical practice (2023). National Health Care Institute. Via: www.zorginstituutnederland.nl.

effectiveness[3], necessity[4] and feasibility[5]. The Scientific Advisory Board (WAR) advises the National Health Care Institute on the (scientific) basis and the conclusion of the assessment. Interested parties were also consulted in this context.

Since glofitamab does not meet the legal criterion of 'the established medical science and medical practice' for the relevant indication, the full weighting of the four package criteria and advice from the Insured Package Advisory Committee (ACP) is not relevant in this case.

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Comprehensive weighting of package criteria

Established medical science and medical practice
DLBCL is a type of lymphoma. It belongs to the group of non-Hodgkin lymphomas. The standard first-line treatment of DLBCL consists of immunochemotherapy with an R-CHOP regimen consisting of **r**ituximab in combination with **c**yclophosphamide, **h**ydroxydaunomycin, vincristine (**O**ncovin®) and **p**rednis(ol)one, respectively. Second-line and third-line treatment depends (partially) on the patient's age and level of fitness. It can consist of chemotherapy, radiation, stem cell transplantation or CAR-T cell therapy (or a combination of these). Since 2021, if patients are not eligible for stem cell therapy or CAR-T cell therapy, they can be treated with the combination of **pola**tuzumab vedotin with **b**endamustine and **r**ituximab (Pola-BR; Polivy®).

Glofitamab is indicated as monotherapy for the treatment of adult patients with R/R DLBCL after two or more lines of systemic therapies. Its efficacy and safety were studied in a single-arm, open-label, multicentre phase I/II study (NPO30179). In this study, patients aged ≥18 years with R/R DLBCL who had previously received at least two systemic therapies were treated with glofitamab monotherapy. No direct comparative study has been conducted with Pola-BR. The marketing authorisation holder has therefore indirectly compared glofitamab and Pola-BR. The outcome has not been published. The National Health Care Institute has therefore performed its own naive indirect comparison. This letter is confined to the main conclusions. For more detailed information, please consult the pharmacotherapeutic report.

In the interim analysis, which was the starting point for the SmPC, overall survival (OS) in glofitamab-treated patients was 11.5 months (95% CI; 7.9 – 15.7) after a follow-up duration of 12.6 months. In Pola-BR, this was 12.4 months (95% CI; 9.0 – 32.0) after a follow-up duration of 48 months. Progression-free survival (PFS) was 4.9 months for glofitamab and 9.2 months for Pola-BR. It was not possible to make a statement on the mutual difference in effect on quality of life.

In February 2023, the National Health Care Institute concluded that the medicinal product Minjuvi® [tafasitamab (TAFA) in combination with lenalidomide (LEN), TAFA-LEN] has a therapeutic equivalent value to Pola-BR in patients with R/R DLBCL. In the naive indirect comparison with Pola-BR, TAFA-LEN had similar uncertainties about the evidence of effectiveness as is now the case for

[3] Cost-effectiveness report (2015).. National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl.
[4] Necessity deals with both the medical necessity and the result of 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).
[5] The package criterion of feasibility deals with whether it is feasible or sustainable to include a specific form of care in the basic health care package. It is therefore mainly a test of a number of implementation aspects, such as the health care organisation, the support base, ethical and legal aspects, budget impact, etc. See the report on real-world package management 4 (2023).

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glofitamab. However, OS for TAFA-LEN was so high at 33.5 months that the National Health Care Institute concluded a similar value to Pola-BR. In contrast, OS for glofitamab is not only significantly lower than OS for TAFA-LEN, but also lower than OS for Pola-BR. Based on the available data and the methodological deficiencies of this indirect comparison between glofitamab and Pola-BR, the National Health Care Institute cannot conclude with sufficient confidence that these products have an equivalent value. For that reason, glofitamab does not meet the established medical science and medical practice for adult patients with R/R DLBCL who have previously received at least two systemic therapies. It is important to note that the professional association supports this conclusion in the consultation.

Budget impact
Because glofitamab does not meet the established medical science and medical practice, no budget impact analysis was performed.

Conclusion
The National Health Care Institute advises you to not include glofitamab in the health insurance package for the treatment of adult patients with R/R DLBCL who have previously received at least two systemic therapies.

Yours sincerely,

Sjaak Wijma
Chairperson of the Executive Board