Zorginstituut Nederland

> Return address PO Box 320, 1110 AH Diemen

To the Minister of Health, Welfare and Sport
P.O. Box 20350
2500 EJ THE HAGUE

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
A. de Waal
warcg@zinl.nl

Our reference
2025007971

2025007971

Date 11 April 2025
Re: Advice on the reassessment of lock procedure medicinal product abemaciclib (Verzenios®) for early-stage breast cancer

Dear Ms Agema,

The National Health Care Institute advises you to not include abemaciclib (Verzenios®) for the treatment of patients with early-stage breast cancer at high risk of recurrence in the healthcare package.

The National Health Care Institute reassessed whether abemaciclib (Verzenios®) can be reimbursed from the basic healthcare package. The reason for this advice was the interim injunction brought by the marketing authorisation holder. Because of the expected high costs, the Minister has placed abemaciclib in the 'lock procedure for expensive medicinal products' for this indication.

Breast cancer is the most common form of cancer in women in the Netherlands. Breast cancer also occurs in men. There are about 15,000 new patients a year. Breast cancer is called 'early-stage' when it has not yet metastasised. The treatment of early-stage breast cancer is focused on curing. Many of these people have a good life expectancy. They are adequately helped by existing treatments that are already reimbursed, including surgery, chemotherapy and possibly radiotherapy. The medicinal product under assessment here is specifically targeting patients with a specific subtype with a high risk of disease recurrence. Approximately 13% of these people have a high risk of disease recurrence when diagnosed. The existing treatments are not always sufficient to help them. Of these patients, about 1 in 3 has died after ten years (10-year survival 63.4%). These patients require better or additional treatments that increase survival.

Registered indication
Abemaciclib, in combination with endocrine therapy, is indicated as adjuvant treatment of adult patients with hormone receptor (HR)-positive human epidermal growth factor receptor 2 (HER2)-negative, node-positive early breast cancer with a high risk of recurrence.

In addition, abemaciclib is also registered for advanced or metastatic breast cancer. This indication is already reimbursed and is therefore not taken into account.

Claim from the marketing authorisation holder
Abemaciclib has added value for the registered indication compared to endocrine therapy alone.

National Health Care Institute
Care
Medicinal Products

Date
11 April 2025

Our reference
2025007971

Package advice

The National Health Care Institute recommends that abemaciclib in combination with endocrine therapy for the adjuvant treatment of adult patients with hormone receptor (HR) positive human epidermal growth factor receptor 2 (HER2) negative, node-positive early-stage breast cancer with a high risk of recurrence should not be included in the basic healthcare package. The National Health Care Institute has established that abemaciclib does not meet the legal criterion of 'established medical science and medical practice' for this indication.

We explain the preparation of this package advice below.

General
At your request, from the point of view of the basic healthcare package paid from joint premiums, the National Health Care Institute assesses whether certain healthcare should be part of the health insurance package.

The National Health Care Institute assesses on the basis of the four package criteria[1]: effectiveness[2]cost-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. Stakeholders are consulted during the process.

Since abemaciclib does not meet the legal criterion of 'established medical science and medical practice' for the above indication, an integral weighting of the four package criteria and advice by the Package Advisory Committee (ACP) is not warranted.

The National Health Care Institute carried out the reassessment of abemaciclib thoroughly and carefully, with a new assessment team. A start-up meeting was organised with representatives of the professional association, the guideline committee, the patient associations and the Association of Dutch Healthcare Insurers. The marketing authorisation holder submitted new study results. The reassessment did not take into account the initial assessment. All arguments have been re-weighted. All stakeholders were consulted for the reassessment report. The substantive arguments put forward have been responded to and relevant substantive comments have been incorporated into the reassessment report. The National Health Care Institute has carefully justified the considerations and choices in the reassessment report.

---

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

[2] Assessment of the established medical science and medical practice (2023). National Health Care Institute. Via www.zorginstituutnederland.nl.

[3] Healthcare cost-effectiveness report (2024) National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl.

[4] 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).

[5] 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).

National Health Care Institute
Care
Medicinal Products

Date
11 April 2025

Our reference
2025007971

Substantive assessment

Established medical science and medical practice

The international, open-label, randomised study monarchE studied abemaciclib added to endocrine therapy compared to endocrine therapy alone in patients with HR-positive, HER2-negative, node-positive early-stage breast cancer with a high risk of recurrence. At a median follow-up of ~54 months, 197 of 2,555 patients (7.7%) died in the abemaciclib arm, and 223 of 2,565 patients (8.7%) in the control arm. The effect on overall survival was not statistically significantly different between patients treated with abemaciclib and patients treated without the addition of abemaciclib (hazard ratio [HR] 0.89; 95% confidence interval [CI]: 0.74 – 1.08]). The effect of abemaciclib relative to the control group also does not meet the minimal clinically important difference (MCID) for adjuvant treatments as stated by the Oncological Medicines Assessment Committee (cieBOM) and used by the National Health Care Institute in the adjuvant treatment assessment (5% difference or 3% and HR < 0.70 for overall survival with a median follow-up of at least 3 years).

Invasive disease-free survival was also considered as a surrogate outcome[6] for survival. This is because survival data are still immature[7] and mature survival data from appropriate studies are not reasonably expected at this time. Invasive disease-free survival measures the time to the return of the cancer or death. The effect of abemaciclib on invasive disease-free survival also does not meet the MCID for adjuvant treatments set by the cieBOM for a preliminary positive advice.

The National Health Care Institute concludes that, based on both the directly measured survival data and the surrogate outcome invasive disease-free survival, there is no demonstrated clinically relevant effect of abemaciclib on survival.

Long-term quality of life (12 months after completion of treatment) appears to be maintained after the addition of abemaciclib to endocrine therapy. Toxicity, including serious adverse effects, increased to a clinically relevant extent during treatment. The number of patients who discontinued treatment due to these adverse events also increased to a clinically relevant extent. In the absence of a clinically relevant improvement of the beneficial effects, a clinically relevant increase of adverse effects is unacceptable.

WAR advice

The reassessment report has been discussed twice in the Scientific Advisory Board (WAR) in accordance with our assessment process. The WAR has advised in both meetings that abemaciclib does not meet the established medical science and medical practice.

[6] A surrogate outcome is an event that can be measured more easily or earlier than the hard outcome. For example: people often experience a recurrence of the cancer first (surrogate outcome) and may die afterwards (hard outcome). A valid surrogate predicts the effect on the hard outcome.

[7] Overall survival data are still immature. This means that the planned final analysis of the monarchE study, that will take place after either 650 events or after 10 years, has not yet taken place.

In conclusion
Based on available data, abemaciclib does not meet the established medical science and medical practice as an adjuvant treatment for HR+/HER2- node-positive early-stage breast cancer with a high risk of recurrence.

Should you need any further information, please do not hesitate to contact us. The pharmacotherapeutic report is attached.

Yours sincerely,

M.J. Janssen
Chairperson of the Executive Board

National Health Care Institute
Care
Medicinal Products

Date
11 April 2025

Our reference
2025007971