Abemaciclib (Verzenios®) for the treatment of metastatic breast cancer

Summary of recommendations by *Zorginstituut Nederland* (National Health Care Institute, the Netherlands) dated 7 March 2019

Zorginstituut Nederland carried out an assessment of the medicinal product abemaciclib (Verzenios®) and came to the following conclusion.

On 27 August 2018, the Minister of VWS placed abemaciclib for the indication metastatic breast cancer in the "waiting room" or "*sluis*", due to the high macro-costs expected. *Zorginstituut Nederland* has completed its assessment of abemaciclib (Verzenios®) for the indication metastatic breast cancer.

Abemaciclib, a selective inhibitor of cycline-dependent kinases 4 and 6 (CDK4/6) is indicated for the treatment of women with hormone receptor (HR)-positive, human epidermal growth factor 2 (HER2)-negative locally advanced or metastatic breast cancer:

- in combination with an aromatase inhibitor or fulvestrant as initial endocrine-based therapy, or in women who have previously received endocrine therapy.

The *Zorginstituut* assessed abemaciclib based on the package criteria[1] effectiveness,[2] cost-effectiveness,[3] necessity and feasibility. Assessing from the perspective of the basic insured health care package that is paid from collective premiums, the *Zorginstituut* decides whether new care is better than what is currently available. In doing this we look at the degree of certainty that has been achieved, both from a scientific perspective, and in relation to societal support. This letter is to inform the Minister about the results of our integral assessment of these package criteria. The *Zorginstituut* was advised by two independent committees: the Scientific Advisory Board (WAR), which examines the data on established medical science and medical practice and determines the cost-effectiveness, and the Insured Package Advisory Committee (ACP), which considers the societal assessment. Stakeholders are also consulted during the process.

Integral consideration of the package criteria and package advice
Abemaciclib, in combination with endocrine therapy, complies with the statutory criterion 'established medical science and medical practice' for patients with hormone-receptor positive, HER2-negative, advanced or metastatic breast cancer who were not previously treated with endocrine treatment (first line), or for patients who did receive prior endocrine therapy (second line). Based on indirect comparisons, we conclude that there are probably no clinically relevant differences in favourable and unfavourable effects between abemaciclib and the other CDK4/6 inhibitors, ribociclib (Kisqali®) and palbociclib (Ibrance®), which were already accepted into the insured health care package in earlier 'waiting-room' procedures on 1 August 2017 and 1 May 2018 respectively. In daily clinical practice, this will enable medical professionals to select one of the three products

[1] Package Management in Practice 3 (2013). Zorginstituut Nederland, Diemen. Via www.zorginstituutnederland.nl

[2] Assessment of Established Medical Science and Medical Practice: updated version (2015). Zorginstituut Nederland, Diemen. Via www.zorginstituutnederland.nl

[3] Cost-effectiveness report (2015). Zorginstituut Nederland, Diemen. Via www.zorginstituutnederland.nl

for individual patients or subpopulations.

The costs per patient per day, using the official list prices, amount to €96.43, €94.82 and €80.32 for abemaciclib, ribociclib and palbociclib respectively. Based on the official list prices, the costs of treatment with abemaciclib are higher than those of ribociclib and palbociclib. However, we have no information on the actual prices of ribociclib and palbociclib due to the confidentiality of the financial agreements made by the Minister.

Based on the official list prices, using abemaciclib for the above-mentioned indications will result in additional costs that are estimated at €3.26 million annually. This assumes equal market penetration by the three products. Various uncertainties are involved, such as the number of patients who will actually be treated with a CDK4/6 inhibitor. Furthermore, at this moment, it is not clear what market shares abemaciclib, ribociclib and palbociclib will have. As a consequence, the extent of the additional costs of abemaciclib is not clear.

As this is the third selective, reversible CDK4/6 inhibitor, and based on the assumption that no relevant clinical differences exist between the three products, we did not carry out a cost-effectiveness analysis.

In view of the high budget impact of abemaciclib, and in the light of the availability of ribociclib and palbociclib – for which a financial arrangement exists – the *Zorginstituut* states that the current price of abemaciclib is unacceptable. In consultation with the Insured Package Advisory Committee (ACP), we advise the Minister to include abemaciclib in the same financial arrangement as ribociclib and palbociclib. When this arrangement ends (i.e. by 31 December 2020[4]), the products should be able to compete with one another.

Appropriate use
The specialists have indicated that abemaciclib will be used in the current SONIA study after approval for inclusion in the insured package. This study is examining whether CKD4/6 inhibitors can best be used as initial treatment or as follow-up treatment. Although the SONIA study was not set up to study the effectiveness of the two products, the *Zorginstituut* concludes that this study deals with the most important questions raised about appropriate use and (cost)-effectiveness. The *Zorginstituut* is following and monitoring this study.

Evaluation
If abemaciclib is accepted into the insured package based on the outcome of the price negotiations, the *Zorginstituut* will actively monitor its use, as well as that of ribociclib and palbociclib. The *Zorginstituut* plans to inform the Minister in 2021 about the results of these measurements. The *Zorginstituut* will monitor the following:

- The extent to which the originally estimated number of patients agrees with the number of patients actually treated;
- Cost developments relative to the original estimation, part of which is formed by monitoring the actual price of abemaciclib;

[4] Central Government, overview of current financial arrangements and (current) waiting room procedures, 2 October 2018. Via: https://www.rijksoverheid.nl/documenten/publicaties/2018/10/02/lopende-financiele-arrangementen-en-aangekondigde-sluisprocedures

- Frequency and duration of the treatment in order to assess appropriate use.

If this monitoring indicates strong discrepancies from current estimates, this may give reason for the *Zorginstituut* to reassess the position of abemaciclib within the field of metastatic breast cancer.

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The original text of this excerpt from advice of Zorginstituut Nederland was in Dutch. Although great care was taken in translating the text from Dutch to English, the translation may nevertheless have resulted in discrepancies. Rights may only be derived on the basis of the Dutch version of Zorginstituut Nederland's advice.
Furthermore, Zorginstituut Nederland points out that only the summary of this report was translated. A proper understanding of all relevant considerations and facts would require familiarity with the Dutch version of this report, including all appendices.