Zorginstituut Nederland

> Return address PO Box 320, 1110 AH Diemen

To the Minister of
Health, Welfare and Sport
PO Box 20350
2500 EJ THE HAGUE

2021049295

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
Dr T.H.L. Tran
T +31 (0)6 120 014 12

Our reference
2021049295

Date 17 January 2022
Subject Package advice tucatinib (Tukysa®)

Dear Mr Kuipers,

The National Health Care Institute advises you on tucatinib (Tukysa®) in combination with trastuzumab and capecitabine for the treatment of adult patients with locally advanced or metastatic HER2-positive breast cancer who have received at least two prior anti-HER2 treatment schedules. The reason for this advice is that tucatinib is being placed in the lock procedure for expensive medicinal products.

The National Health Care Institute has concluded that tucatinib in combination with trastuzumab and capecitabine meets the legal criterion of 'established medical science and medical practice' for the indication mentioned. It is considered an effective treatment combination that provides a clinically relevant gain in overall survival. However, it is not a cost-effective treatment and it also involves significant additional costs for the health insurance package.

The National Health Care Institute recommends including tucatinib in combination with trastuzumab and capecitabine in the package, provided a price reduction of at least 65% can be achieved.

We would like to explain our findings and final conclusion below.

General
At your request, the National Health Care Institute assesses whether new care should be part of the health insurance package, and makes a decision based on the health care package paid from joint premiums. We take into consideration the degree of certainty that this will be achieved, both in the scientific sense, as well as in terms of social support, and we consider the efficiency and transparency aspects.

The National Health Care Institute has assessed tucatinib in combination with trastuzumab and capecitabine for the indication mentioned on the basis of the

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four package criteria[1]: effectiveness[2], cost-effectiveness[3], necessity and feasibility. The National Health Care Institute is advised by the Scientific Advisory Board (WAR) for advice on established medical science and medical practice and on cost-effectiveness, and the Insured Package Advisory Committee for the social assessment. We also consulted stakeholders during the assessment process.

Integral weighting of package criteria

Established medical science and medical practice

Tucatinib (Tukysa®) was studied in the randomized HER2CLIMB study and compared to placebo, in both treatment arms as an addition to trastuzumab and capecitabine. Based on this study, it can be concluded that tucatinib as an addition to trastuzumab and capecitabine has a clinically relevant effect on overall survival. Treatment with tucatinib resulted in a 34% lower risk of death compared to a placebo, as an addition to trastuzumab and capecitabine (Hazard Ratio [HR] 0.66; 95% BI: 0.50-0.88). The absolute difference in median survival was 4.5 months in favour of tucatinib. This means that patients live longer when tucatinib is added to the combination of trastuzumab and capecitabine. The median progression-free survival rate significantly increased by 2.2 months (HR 0.54; 95% BI: 0.42-0.71). In the pre-specified subgroup with brain metastases, the difference in median PFS was also 2.2 months (HR 0.48; 95% BI: 0.34– 0.69). Both the absolute gain in overall survival and the relative effect estimate meet the PASKWIL criteria (palliative, adjuvant, specific side effects, quality of life, impact of treatment and level of evidence) for clinically relevant effect.

Severe intervention-related undesirable effects were more common during treatment with tucatinib as an addition to capecitabine and trastuzumab, but the incidence of treatment cessation due to undesirable effects was low, both during treatment with tucatinib (4%) and in the placebo group (2.5%). In addition, the study showed no indication of deterioration in quality of life as a result of the addition of tucatinib to the usual treatment with trastuzumab and capecitabine. In relation to the desirable effects, the National Health Care Institute therefore considers the undesirable effects to be acceptable.

Budget impact

Treatment with tucatinib in combination with trastuzumab and capecitabine for the treatment of metastatic HER2-positive breast cancer patients who have received at least two prior HER2-focused treatments costs €84,983 per patient. The additional costs of tucatinib combined with trastuzumab and capecitabine are estimated to be €14 million in the third year after inclusion in the package. This is based on the expectation that 218 patients will be treated in the third year.

Cost-effectiveness

The cost-effectiveness analysis provided is of sufficient methodological quality. The incremental cost-effectiveness ratio (ICER) has been determined as €208,439 per QALY. This means that treatment with tucatinib in combination with trastuzumab and capecitabine is not cost-effective and the price would have to

[1] Real-world package management 3 (2013). National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl

[2] Established medical science and medical practice assessment: updated version (2015). National Health Care Institute,
Diemen. Via www.zorginstituutnederland.nl

[3] Cost-effectiveness report (2015). National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl

decrease by at least 65% if it is to fall below the reference value of €80,000 per QALY.

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Package advice
The National Health Care Institute recommends including tucatinib in combination with trastuzumab and capecitabine for the above indication in the package, provided a price reduction of at least 65% can be achieved.

Evaluation
If tucatinib in combination with trastuzumab and capecitabine is added to the health insurance package, the National Health Care Institute will monitor the use of the combination mentioned. We will inform you about our findings no later than 2025.
In the context of the treatment landscape, the National Health Care Institute will then consider the following:

- the initial estimate of the number of patients compared to the actual number treated;
- the cost development compared to the original estimate.

Yours sincerely,

Sjaak Wijma
Chair of the Executive Board