Zorginstituut Nederland

> Return address PO Box 320, 1110 AH Diemen

Minister of Medical Care and Sport
PO Box 20350
2500 EJ THE HAGUE

2021041515

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
2021041515

Date 15 November 2021
Subject Osimertinib (Tagrisso®) as adjuvant treatment after complete tumour resection in adults with stage IB-IIIA NSCLC with EGFR mutations

Dear Mr Blokhuis,

The National Health Care Institute advises you on osimertinib (Tagrisso®) as monotherapy in adjuvant treatment after complete tumour resection in adult patients with stage IB-IIIA non-small cell lung cancer involving tumours with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L585R) substitution mutations. The reason for this advice was the placement of the said medicinal product in the lock procedure for expensive medicinal products.

The National Health Care Institute has concluded that osimertinib meets the statutory criterion of 'established medical science and medical practice' for the said indication. This is an effective medicinal product that substantially prolongs the disease-free interval. This is a cost-effective medicinal product for the said indication, but there are arguments to advise you to negotiate the price. We therefore advise you to include osimertinib in the health insurance package for the said indication, provided that the price negotiations with the marketing authorisation holder result in a lower price that is at least in line with the current price arrangement.

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 public support, and we consider the efficiency and transparency aspects.

National Health Care Institute
Care
Medicinal Products

Date
15 November 2021

Our reference
2021041515

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

Integral weighting of package criteria

Established medical science and medical practice
The standard treatment for resectable non-small cell lung cancer is surgical removal of the tumour with systematic mediastinal lymph node dissection. This treatment is considered to be a curative treatment. Tumour resection, possibly followed by adjuvant chemotherapy, is followed by an active surveillance policy. For the said indication, osimertinib – an EGRF tyrosine kinase inhibitor (TKI) – has been investigated in a single randomized, controlled, phase 3 study (ADAURA), with the active surveillance policy as a comparative arm.
The results are based on an unplanned interim analysis involving immature data. The data from the ADAURA study are too immature for any firm conclusions to be drawn about the effect of osimertinib on overall survival. The effect of osimertinib on overall survival is still very uncertain. It is also uncertain whether treatment with osimertinib impacts a patient's quality of life.
The results of the unplanned interim analysis have already shown that osimertinib has a clinically relevant effect on disease-free survival. This means that osimertinib provides a longer delay in the recurrence of the disorder than when an active surveillance policy is used. In this way, it delays progression to a potentially much more severe clinical picture. Median disease-free survival had not yet been reached in the osimertinib group. In the active surveillance arm, however, median disease-free survival had already been reached, and was 27.5 months. This gives a hazard ratio (HR) of 0.20 (99.12% CI: 0.14-0.30), which complies with the Oncological Medicines Assessment Committee's PASKWIL criteria (palliative, adjuvant, specific side effects, quality of life, impact of treatment and level of evidence) for adjuvant treatment. The immaturity of the data is sufficient reason for the Oncological Medicines Assessment Committee to deem its positive recommendation concerning osimertinib to be provisional at this stage. It is anticipated that further analyses, based on more mature data, will be conducted in 2024.

Osimertinib elicits a range of common undesirable effects, including diarrhoea, rash, paronychia, dry skin, and stomatitis. Treatment with osimertinib resulted in more intervention-related undesirable effects, and more patients discontinued treatment than those who were being managed solely by means of an active surveillance policy. However, both incidences are still low (<10%).

[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

The National Health Care Institute has concluded that osimertinib as monotherapy in adjuvant treatment after complete tumour resection in adult patients with stage IB-IIIA non-small cell lung cancer involving tumours with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L585R) substitution mutations has added therapeutic value as compared to the active surveillance policy. Osimertinib is, therefore, in line with established medical science and medical practice. The said uncertainties were taken into account in the assessment concerning established medical science and medical practice.

National Health Care Institute
Care
Medicinal Products

Date
15 November 2021

Our reference
2021041515

Budget impact
Applying osimertinib for the said indication will involve additional costs estimated at €13.9 million in the third year after inclusion in the package. This concerns 79 patients in the first year, rising to 106 patients in the third year.

Cost-effectiveness
The cost-effectiveness analysis provided is of sufficient methodological quality. Compared to active surveillance, the incremental cost-effectiveness ratio (ICER) is €14,884 per quality-adjusted life year (QALY). It is cost effective at the relevant reference value of €50,000 per QALY.

Other considerations
Osimertinib is already reimbursed for various indications, including the primary care treatment of adult patients with locally advanced or metastatic non-small cell lung cancer with activating EGFR mutations. A financial arrangement has been concluded for this indication, and will remain in effect until 2024.
The current assessment involves a shift of the use of osimertinib to an earlier point in the treatment and at an earlier stage of the disorder. There is some uncertainty about whether the earlier use of osimertinib ultimately delivers an overall survival gain, compared to the current treatment algorithm, in which osimertinib is used at a later point.

Package advice
The National Health Care Institute advises you to include osimertinib in the health insurance package, provided that the price negotiations with the marketing authorisation holder result in a lower price that is at least in line with the current price arrangement. This is an effective medicinal product with a favourable cost-effectiveness profile. However, there are uncertainties about the potential survival gains, the quality of life, and the duration of the treatment. We have taken these uncertainties into account in our advice. Accordingly, the National Health Care Institute advises you to negotiate a price. In addition, osimertinib is already being reimbursed for several indications. This means that the marketing authorisation holder has already been largely compensated for the efforts they have had to make to market the product. This supports the argument that a lower price can – and must – be paid.
If mature data become available on overall survival, quality of life and duration of treatment, the National Health Care Institute will reassess osimertinib for the said indication, if necessary.

National Health Care Institute
Care
Medicinal Products

Date
15 November 2021

Our reference
2021041515

Appropriateness and registration
When considering the use of osimertinib as adjuvant treatment after complete tumour resection in patients with non-small cell lung cancer, their eligibility for osimertinib treatment must be established. To this end, it is important to demonstrate (by means of a validated test performed in a clinical laboratory) that the tumour tissue has a positive EGFR mutation status. In the light of past experience with the testing and use of EGFR-TKIs, the National Health Care Institute does not expect any relevant risks with regard to appropriateness. Osimertinib treatment should be continued until the disorder recurs or until unacceptable toxicity occurs. As yet, however, no studies have addressed treatment durations in excess of three years.

The Netherlands has no national lung cancer registry for the collection of data to adequately monitor the effective use of such treatment. Given the large number of expensive medicinal products used in the treatment of lung cancer, the National Health Care Institute feels that it is important to establish a national lung cancer registry.

Evaluation
If osimertinib for the said indication is added to the health insurance package, the National Health Care Institute will monitor the use of this medicinal product. We will inform you about our findings no later than 2025. In the context of the treatment landscape, the National Health Care Institute considers the following points:

- 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