Zorginstituut Nederland

Durvalumab (Imfinzi®) for the treatment of locally advanced, unresectable, non-small cell lung cancer

Summary of recommendations by *Zorginstituut Nederland* (National Health Care Institute, the Netherlands) dated 1 April 2019

Zorginstituut Nederland carried out an assessment of the medicinal product durvalumab (Imfinzi®), whereby the following conclusion was drawn.

Zorginstituut Nederland has completed its assessment of durvalumab (Imfinzi®) as monotherapy for the treatment of locally advanced, unresectable, non-small cell lung cancer (NSCLC). The Minister of Health, Welfare and Sport (VWS) has placed durvalumab in the so-called 'waiting room' or 'sluice' for expensive drugs.

The *Zorginstituut* assessed durvalumab based on the four package criteria,[1] effectiveness,[2] cost-effectiveness,[3] necessity and feasibility. Assessing from the perspective of the basic package which is paid from collective premiums, the *Zorginstituut* evaluates whether the new drug is better than the currently available care. In doing this we look at the degree of certainty that this will be achieved, both from a scientific perspective, and in relation to societal support. The *Zorginstituut* is 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. Interested parties are also consulted during the process. This letter is to inform the Minister about the results of our integral assessment of these package criteria.

Integral consideration of the package criteria and package advice

Durvalumab complies with the statutory criterion, 'established medical science and medical practice', for the treatment of adult patients with locally advanced, unresectable (stage III), non-small cell lung cancer (NSCLC), and with ECOG performance status 0-1, in whom there is no evidence of disease-progression following concomitant platinum-containing chemotherapy with radiotherapy, irrespective of the tumour's PD-L1 expression.

Durvalumab is an immunotherapy (PD-L1-inhibitor) that aims to improve the immune system's anti-tumour response. It is administered by intravenous infusion. It has the potential of being a curative treatment for a sub-group of patients with a high burden of disease (0.83) for whom no curative treatment is yet available. The current standard treatment of inoperable stage III NSCLC, after concomitant chemotherapy with radiotherapy, is active monitoring until disease progression occurs.

In a randomised, clinical trial, after a median follow-up of 25.2 months, treatment with durvalumab achieved an increase in overall survival of *at least* 6.0 months in comparison with the standard treatment. This is a conservative estimate because the median survival in the durvalumab arm has not yet been achieved. The unintended effects of durvalumab are mostly immune-mediated reactions and

[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

infections. As durvalumab has a manageable safety profile, the *Zorginstituut* finds the unintended effects acceptable.

The treatment costs with durvalumab in cases of locally advanced, unresectable NSCLC where there was no evidence of disease-progression after concomitant chemotherapy with radiotherapy are €61,758 per patient. The additional costs to the pharmacy budget if durvalumab is accepted into the basic package are estimated at €52.3 million in the third year after its inclusion (incl. the costs of administering durvalumab: €56.8 million). This is inclusive of follow-up treatment costs.

The *Zorginstituut* concluded that the cost-effectiveness analysis supplied by the manufacturer is of sufficient methodological quality. Determination of the cost-effectiveness shows a favourable estimated cost-effectiveness of €35,000 per QALY. A reference value of €80,000/QALY is deemed relevant for patients with this high burden of disease.

Within this framework, the *Zorginstituut* assessed in particular two aspects in arriving at its advice for the Minister. In connection with the high budget impact and the expectation that this drug will also be used for other indications or earlier treatment lines, which will increase the volumes, the *Zorginstituut* advised the Minister to negotiate on durvalumab's price. A price-volume agreement seems the logical choice, in view of the realistic chance of an indication extension.

Furthermore, within the framework of improving the appropriate use of durvalumab and similar drugs, the *Zorginstituut* advises the Minister to carry out further research into PD-L1 expression, or to promote and structurally organise other prognostic tumour markers.

Appropriate use
The NVALT has stated that durvalumab will be included in the guidelines on treating NSCLC, with start criteria in line with those in the phase 3 study that was carried out with this drug. Durvalumab will only be used in centres that fulfil the NVALT's criteria for using immunotherapy.

Evaluation
If durvalumab is accepted into the insured package based on the outcome of price negotiations, the *Zorginstituut* will actively monitor its use. The *Zorginstituut* plans to inform the Minister in 2022 about the results of these measurements.

The Zorginstituut will be assessing, among other things:

- 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 durvalumab;
- Care consumption with a view to assessing the points of departure for appropriate use.

If this monitoring indicates strong discrepancies from the current estimates, this can be a reason for the *Zorginstituut* to reassess the position of durvalumab.

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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.