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Our reference
2021025280

Date 21 July 2021
Subject Package advice for avelumab (Bavencio®) for treating urothelial cell carcinoma

Dear Ms van Ark,

The National Health Care Institute is hereby advising you about avelumab (Bavencio®) as monotherapy for the primary-care maintenance treatment of adult patients with locally advanced or metastatic urothelial cell carcinoma who are progression-free after platinum-based chemotherapy. The reason for this advice was that the said medicinal product was being placed in the so-called 'package lock' for expensive medications.

The National Health Care Institute has concluded that avelumab meets the statutory criterion of 'established medical science and medical practice' for the indication mentioned. This is an effective medicine that significantly prolongs patients' lives. However, the budgetary impact is high and unfavourable in terms of cost-effectiveness. The National Health Care Institute recommends that you should include avelumab in the health care package for the above-mentioned indication if a price reduction of at least 30% can be achieved.

I 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 basic insured 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. 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 appraisal. We also consulted stakeholders during the assessment process.

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The National Health Care Institute has assessed avelumab on the basis of the four package criteria[1] of effectiveness[2], cost-effectiveness[3], necessity and feasibility.

Integral weighting of package criteria

Established medical science and medical practice
Based on the randomised, controlled, open-label phase III JAVELIN Bladder 100 study, the median overall survival was 21.4 months (95% CI 18.9–26.1) in the avelumab arm and 14.3 months (95% CI 12.9–17.9) in the 'best supportive care' arm. This boils down to a relative effect estimate – the hazard ratio – of 0.69 (95% CI 0.56– 0.86). Both the absolute gain in overall survival (7.1 months) and the relative effect estimate meet the PASKWIL criteria (palliative, adjuvant, specific side effects, quality of life, impact of treatment and level of evidence) of the BOM committee (Oncological Medicines Assessment Committee). The effect of avelumab on overall survival is therefore clinically relevant.

Treatment with avelumab resulted in more intervention-related adverse events (grades 3 and 4) and more patients discontinued treatment than among patients receiving best supportive care alone. However, this did not lead to deterioration in the quality of life. In relation to the desirable effects, the National Health Care Institute therefore considers the adverse effects to be acceptable. This is an effective medicine that significantly prolongs the patients' lives.

The final conclusion reached by the National Health Care Institute is that avelumab as monotherapy for the primary-care maintenance treatment of adult patients with locally advanced or metastatic urothelial cell carcinoma who are progression-free after platinum-based chemotherapy has added value with respect to the best supportive care. Avelumab is therefore in line with established medical science and medical practice.

Budget impact
Applying avelumab for the indication mentioned above will mean additional costs estimated at €20.9 million in the third year after inclusion in the package.

Cost-effectiveness
The National Health Care Institute considers the cost-effectiveness analysis of avelumab compared to the best supportive care to be sufficient in terms of quality. The incremental cost-effectiveness ratio (ICER) has been determined as €112,705 per QALY. This means that treatment with avelumab is not cost-effective and the price would have to decrease by at least 30% if it is to fall below the reference value of €80,000 per QALY.

Package advice

The National Health Care Institute recommends that you should include avelumab in the health care package for the above-mentioned indication if a price reduction

[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

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of at least 30% can be achieved.

Effective use
The physicians association has indicated that it will conduct an efficiency study to see whether the same treatment results can be achieved with a shorter treatment duration and if it is possible to predict which patients will respond to the medication. The National Health Care Institute therefore is confident that the occupational group will use avelumab effectively. The National Health Care Institute applauds such initiatives, although it has also received signals that the funding for this type of research is often a bottleneck. We would like to draw your attention to this bottleneck and ask you to examine – in more general terms as well – how funding can be made available for this kind of efficiency research.

Evaluation
If avelumab is included in the health insurance package, the National Health Care Institute will actively monitor its use. We will inform you about our findings by 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.

In addition, the National Health Care Institute will include the results of the efficiency study in the evaluation.

Yours sincerely,

Tiana van Grinsven
Acting Chair of the Executive Board