National Health Care Institute

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National Health Care Institute
Care
Medicinal Products

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Contact
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2024023811

Date 10 July 2024

Re: Package advice lock procedure medicinal product dostarlimab (Jemperli®)

Our reference
2024023811

Dear Ms Agema,

The National Health Care Institute advises you about dostarlimab (Jemperli®) in combination with platinum-containing chemotherapy in the treatment of patients with mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) advanced or recurrent endometrial cancer (EC). The reason for this advice was the placement of dostarlimab in the lock procedure for expensive medicinal products.

We explain the preparation of this package advice below.

Registered indication
Dostarlimab (Jemperli®) is indicated in combination with carboplatin and paclitaxel for the treatment of adult patients with dMMR/MSI-H primary advanced or recurrent endometrial cancer (EC) who are candidates for systemic therapy.

Background
EC is a form of uterine cancer. This type develops in the inner, mucous membrane layer of the womb, or the endometrium. Dostarlimab is a form of immunotherapy, a PD-1 inhibitor, which helps the patient's own immune system to fight cancer cells.
In the Netherlands, the standard treatment of advanced or recurrent EC consists of carboplatin and paclitaxel.

Claim by the marketing authorisation holder
Dostarlimab in combination with platinum-containing chemotherapy for the treatment of patients with dMMR/MSI-H advanced or recurrent EC has an added value compared to the current standard treatment with carboplatin and paclitaxel.

Package advice
The National Health Care Institute advises you to include dostarlimab in combination with platinum-containing chemotherapy for the treatment of patients with dMMR/MSI-H advanced or recurrent EC in the basic health care package.

The National Health Care Institute has established that dostarlimab in combination

with platinum-containing chemotherapy for the above indication meets the legal criterion of 'established medical science and medical practice' and that there is a therapeutic added value compared to the standard treatment with carboplatin and paclitaxel. The cost-effectiveness analysis shows that this is a cost-effective treatment.

Dostarlimab is a PD-1 inhibitor. The National Health Care Institute recently researched additional information to justify the continuation or discontinuation of the price arrangements for the PD-(L)1 inhibitors. The National Health Care Institute recommends that dostarlimab price negotiations should also take into account the guiding principles of the advice on financial arrangements for the other PD (L)1 inhibitors.

We explain the preparation of this package advice below.

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General
At your request, the National Health Care Institute assesses whether care should be part of the standard health insurance package from the perspective of the basic healthcare package paid from joint premiums.

The National Health Care Institute assesses on the basis of the four package criteria[1]: effectiveness[2]cost-effectiveness[3], necessity[4] and feasibility[5]. The Scientific Advisory Board (WAR) advises the National Health Care Institute on the (scientific) basis and the conclusion of the assessment. If there are risks regarding the accessibility and affordability, the assessment of the package criterion of effectiveness (established medical science and medical practice) will be placed in the wider societal context of the four package criteria. The Insured Package Advisory Committee (ACP) advises the Executive Board of the National Health Care Institute in this regard. This appraisal results in the package advice. Stakeholders are consulted during the process.

Background

Comprehensive weighting of package criteria

Effectiveness

Established medical science and medical practice

For the above indication, dostarlimab has been researched in the RUBY study. The addition of dostarlimab to a treatment with paclitaxel and carboplatin resulted, with a median follow-up of 24.8 months, in a clinically relevant effect on overall survival (OS; hazard ratio (HR): 0.30; 95% confidence interval (CI): 0.13-0.70). Given the immaturity of the data, it is not possible to determine the absolute survival gain. After 2 years, 83.3% of patients in the dostarlimab arm and 58.7% of patients in the control arm were still alive. The marketing authorisation holder

[1] Real-world package management 4 (2023). National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl.

[2] Assessment of the established medical science and medical practice (2023). National Health Care Institute. Via www.zorginstituutnederland.nl.

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

[4] Necessity is related to both the medical need due to the severity of a disease for the patient (burden of disease) and the need to insure something. See the report on real-world package management 4 (2023).

[5] The package criterion of feasibility deals with whether it is feasible or sustainable to include a specific form of care in the basic health care package. It is therefore mainly a test of a number of implementation aspects, such as the health care organisation, the support base, ethical and legal aspects, budget impact, etc. See the report on real-world package management 4 (2023).

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provided a clinical study report with longer follow-up data that support the effect of dostarlimab on OS. Quality of Life appears to be maintained in both treatment arms, although dostarlimab is likely to result in a clinically relevant increase in the incidence of intervention-related serious adverse effects and the incidence of discontinuation due to intervention-related adverse effects. Treatment with dostarlimab is primarily associated with immune-related adverse reactions.

Based on the above, the National Health Care Institute concludes that dostarlimab in combination with platinum-containing chemotherapy in the treatment of patients with dMMR/MSI-H advanced or recurrent EC complies with the established medical science and medical practice. There is an added value compared to standard treatment with carboplatin and paclitaxel.

Cost-effectiveness
The National Health Care Institute concludes that the pharmaco-economic analysis is of sufficient quality and that the outcomes of the analysis are sufficient for decision-making. The incremental cost-effectiveness ratio (ICER) calculated by the marketing authorisation holder is €32,928 per *quality-adjusted life year (QALY)* gained. However, the National Health Care Institute believes that the most realistic ICER will be between €46,278/QALY and €70,867/QALY, taking into account the reduction in treatment effect over time (*treatment waning*). At a maximum reference value of €80,000, the National Health Care Institute concludes that dostarlimab in combination with platinum-containing chemotherapy is a cost-effective treatment for patients with dMMR/MSI-H advanced or recurrent EC.

Budget impact analysis
The National Health Care Institute estimates that in the third year following market introduction, 140 patients with this indication will be treated with dostarlimab in combination with platinum-containing chemotherapy. The total costs per patient per year for dostarlimab in combination with carboplatin and paclitaxel are €170,100 at an average treatment duration of approximately 87 weeks. This results in possible macro costs of €19.1 million in the third year. This assumes complete substitution of treatment with carboplatin and paclitaxel alone.

Price arrangements for PD(L)1 inhibitors
In 2023, the National Health Care Institute recommended that, given the current expenditure and expected increase in macro costs by expansion to previous treatment lines and the expansion with a large number of registered indications and products, a centrally negotiated (continued) financial arrangement should be concluded for each of the already available PD-(L)1 inhibitors[6]. Further indication expansions for dostarlimab are expected to follow. Building on the previous advice regarding the PD (L)1 inhibitors, the National Health Care Institute recommends that a financial arrangement be made for dostarlimab, despite the cost-effective use for the indication mentioned.

Should you need any further information, please do not hesitate to contact us. The assessment reports have been added as annexes (pharmacotherapeutic report, budget impact analysis, pharmaco-economic report).

[6] *https://www.zorginstituutnederland.nl/publicaties/adviezen/2023/01/30/advies-pd-l1-remmers-voor-de-behandeling-van-kanker*

Yours sincerely,

Sjaak Wijma
Chairperson of the Executive Board

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