Zorginstituut Nederland

> Return address PO Box 320, 1110 AH Diemen

Minister of Medical Care and Sports
attn. Medical Devices and Technology Directorate
PO Box 20350
2500 EJ THE HAGUE

2020017341

National Health Care Institute
Care II
Cardiovascular & Pulmonary

Willem Dudokhof 1
1112 ZA Diemen
PO Box 320
1110 AH Diemen
www.zorginstituutnederland.nl
info@zinl.nl

T +31 (0)20-7978555

Contact
Dr T.H.L. Tran
T +31 (0)6-12001412

Our reference
2020017341

Date 19 March 2020
Subject Package advice for olaparib (Lynparza®)

Dear Mr Bruins,

The National Health Care Institute (Zorginstituut Nederland) is hereby advising you about olaparib as a monotherapy for the maintenance treatment of adult patients with advanced (FIGO III or IV) BRCA1/2 mutated (germ line and/or somatic), high-grade epithelial carcinoma of the ovaries, tubes or peritoneum that exhibit a full or partial response to primary treatment with platinum-containing therapeutic agents. The reason for this advice was the placing of the said medicinal product in the so-called 'package lock' for expensive medications.

General
From the point of view of the basic package paid from joint premiums, the National Health Care Institute assesses whether new care should be part of the insured package. We weigh this, both scientifically and in terms of societal support, and we weigh aspects of efficiency and transparency. The National Health Care Institute is advised by two independent committees: the Scientific Advisory Council (WAR) for the scientific and practical assessment of the data and the determination of the cost-effectiveness, and the Package Advisory Committee (ACP) for the societal assessment. We also consulted interested parties during the assessment process.

The National Health Care Institute assessed olaparib on the basis of the four package criteria[1]: effectiveness[2], cost-effectiveness[3], necessity and feasibility. Through this letter, I would like to inform you about the result of the full weighing of these package criteria.

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

[2] Current state of science and 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

National Health Care Institute
Care II
Cardiovascular & Pulmonary

Date
19 March 2020

Our reference
2020009519

Integral package criteria weighing

Olaparib meets the legal criterion of 'established medical science and medical practice' for the maintenance treatment of adult patients with advanced (FIGO III or IV) BRCA1/2 mutated (germ line and/or somatic), high-grade epithelial carcinoma of the ovaries, tubes or peritoneum that exhibit a full or partial response to primary treatment with platinum-containing therapeutic agents.

In a randomised study (SOLO1), olaparib was compared against active monitoring, which is the current standard treatment. After a median follow-up period of 41 months, the estimated 3-year progression-free survival was 60% in the olaparib group and 27% in the actively monitored group. (The hazard ratio (HR) was 0.30 (95% CI: 0.23-0.41). The chance of progression-free survival is considerably increased and meets the criteria (palliative, adjuvant, specific side effects, quality of life, impact of treatment, level of evidence) that the Oncological Medicines Assessment Committee (Commissie BOM) has adopted for clinical effects.

It is too early yet to use the data from SOLO1 to make any statement about the effect of olaparib on overall survival. The immaturity of the data is sufficient reason for the Oncological Medicines Assessment Committee to deem its positive recommendation about olaparib to be provisional at this stage. The EMA has required the manufacturer to submit a re-analysis once the data is approximately 60% mature, by no later than 2023.

Applying olaparib for the indication mentioned above will mean additional costs estimated at €8.9 million in the third year after inclusion in the package.
There is uncertainty about the duration of treatment: the treatment should be stopped after 2 years in patients who are showing no indications of a relapse. The therapy can continue after 2 years for patients exhibiting an ongoing partial response.

There are various registered indications for olaparib tablets and capsules that have previously been included automatically in the insurance package as a form of medical specialist care. Olaparib and niraparib, another PARP inhibitor, are already being used for later- stage treatment of the indication being discussed here. The use of olaparib at an earlier stage of treatment for this indication therefore leads to a shift in the costs.

The incremental cost-effectiveness ratio (ICER) has been determined by the applicant as €10,688 per QALY. Based on the disease burden of 0.65, a reference value of €50,000 per QALY is relevant. Given that reference value, the chance that olaparib is cost-effective as compared to active monitoring is 89%. The National Health Care Institute deems the quality of the cost-effectiveness analysis to be sufficient, although there are some important uncertainties in the assessment of the cost-effectiveness. The overall survival data is immature and thereby an uncertain factor in the cost-effectiveness analysis. Sensitivity analyses also show that the cost-effectiveness analysis depends heavily on the percentage of patients who also receive a PARP inhibitor as follow-up treatment.

National Health Care Institute
Care II
Cardiovascular & Pulmonary

Date
19 March 2020

Our reference
2020009519

Package advice:
Like the Oncological Medicines Assessment Committee, the National Health Care Institute sees olaparib as a medication for the indication stated above with both potential and uncertainties. The expected additional costs are €8.9 million. I will reiterate these points once again below:

- The data are too premature to allow any statement about the effect of olaparib on overall survival, resulting in uncertainty about the added value of olaparib in the said stage of treatment in the longer term.
- It is not known how a 2-year duration of treatment is handled in practice.
- It is uncertain how many patients receive a PARP inhibitor as follow-on treatment.
- New therapies will be developed for this condition that will be competitors to this therapy.

After weighing up the 4 package criteria, the National Health Care Institute has decided on the following advice:
The National Health Care Institute recommends that you include olaparib in the package for the above-mentioned indication. Given the considerable gain in progression-free survival, the limited financial risk if it is included in the package and the high likelihood of its being cost-effective, rapid market access for olaparib for the above-mentioned indication is desirable.

The National Health Care Institute also sees that there is uncertainty about olaparib for the stated indication. In that sense, admitting olaparib to the package should be seen as provisional. The National Health Care Institute will proceed with a reassessment at the point when:
- there is a clearer picture of how these uncertainties are developing (gain in survival, duration of the treatment and the number of patients receiving a PARP inhibitor as part of their follow-on treatment as well),
- there are extensions to the indication, or
- other PARP inhibitors receive marketing authorisation

Appropriate use
Before it is possible to commence olaparib for the above-mentioned indication, it must be determined that the patient is indeed has a BRCA1 or BRCA2 mutation; this should be done by means of genetic diagnostics on tumour tissue. These tests are already being done; the organisation of the testing can however vary from one medical centre to the next. The professional groups involved are working on nationwide implementation of a uniform process for timely determination of the mutation.
The National Health Care Institute will enter into discussions with the professional group about appropriateness: about a duration of treatment of two years and the policy regarding the use of a PARP inhibitor as follow-on treatment.

Evaluation
If olaparib is admitted into the insured package, the National Health Care Institute will actively monitor the use of olaparib. We will inform you about our findings in 2023 at the latest.

National Health Care Institute
Care II
Cardiovascular & Pulmonary

Date
19 March 2020

Our reference
2020009519

In the context of the treatment landscape, the National Health Care Institute takes the following points into consideration:

- The initial estimate of the number of patients compared to the actual number treated;
- The cost development compared to the original estimate.
- The use of appropriateness agreements about a treatment duration of two years and the policy regarding the use of a PARP inhibitor as follow-on treatment.

Developments in testing for BRCA1/2 mutations will also be followed closely by the National Health Care Institute.

If this monitoring yields signals that deviate a great deal from the current estimates, this may give the National Health Care Institute cause to reassess the position of olaparib.

Yours sincerely,

Sjaak Wijma
Chair of the Executive Board