HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY
SUMMARY
16 DECEMBER 2020

The legally binding text is the original French opinion version

olaparib
LYNPARZA (100 mg, 150 mg) tablets

New indication

Key points

Favourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use only in the subpopulation of patients with germline BRCA1/2-mutations who have metastatic adenocarcinoma of the pancreas and have not progressed after a minimum of 16 weeks of platinum treatment within a first-line chemotherapy regimen and who are not suitable for continuation of platinum-based chemotherapy.

Unfavourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the rest of the MA population: patients suitable for continuation of platinum-based chemotherapy, in the absence of any available specific data.

What therapeutic improvement?

No clinical added value in the therapeutic strategy.

Role in the care pathway?

According to the European ESMO and American NCCN recommendations, patients with metastatic pancreatic cancer with an ECOG performance score of 0-2 are suitable for systemic chemotherapy. The FOLFIRINOX (5-FU/LV/irinotecan/oxaliplatin) protocol or nab-paclitaxel/gemcitabine combination are recommended.

In the presence of known BRCA 1/2 mutations, the favoured treatment protocols are FOLFIRINOX or modified FOLFIRINOX or Gemcitabine + cisplatin.

The first-line treatment is administered until progression or significant toxicity.

Role of LYNPARZA (olaparib) in the care pathway:

LYNPARZA is a maintenance option for a very limited number of patients. Indeed, in view of the available data, it is only intended for patients with germline BRCA1/2-mutations who have metastatic adenocarcinoma of the pancreas and have not progressed after a minimum of 16 weeks of platinum treatment within a first-line chemotherapy regimen and who are not suitable for continuation of platinum-based chemotherapy. In patients who are responding, it is preferable to maintain chemotherapy until disease progression or inacceptable toxicity. Outside these precise situations, treatment with LYNPARZA has no role in the absence of data.

COMMITTEE'S CONCLUSIONS

Considering all of this information and further to debate and voting, the Committee considers:

Clinical benefit

◗ Metastatic adenocarcinoma of the pancreas is a life-threatening cancer in the short term.

◗ LYNPARZA (olaparib) is a curative treatment.

◗ In view of:
- the available clinical data (improvement in progression-free survival under maintenance treatment with olaparib compared to placebo without demonstration of an improvement in overall survival or quality of life and in a study in which the placebo comparator group is highly debatable), and
- its safety profile (around one in three patients (39.6%) had grade ≥ 3 adverse events),

on the basis of currently available data the efficacy/adverse effects ratio is moderate.

◗ There is a medicinal alternative at this stage of the disease, represented by the continuation of first-line chemotherapy.

◗ LYNPARZA (olaparib) is a maintenance treatment option administered after a minimum of 16 weeks of first-line **platinum-based chemotherapy in patients who are not suitable for continuation of this chemotherapy. Outside this situation, this medicinal product has no role in the absence of available data.**

◗ **<u>Public health impact</u>:**

Considering:
- the seriousness of adenocarcinoma of the pancreas at the metastatic stage,
- the low incidence of the subpopulation of patients with germline BRCA1/2-mutations, estimated to be around 170 to 300 new cases per year,
- the inadequately met medical need in this disease,
- the fact that LYNPARZA (olaparib) provides no response to the identified medical need in view of the available data (improvement in progression-free survival under maintenance treatment with olaparib compared to placebo without demonstration of an improvement in overall survival or quality of life and in a study in which the placebo comparator group is highly debatable), the impact on morbidity and mortality is difficult to quantify in this indication and the impact on quality of life is not demonstrated,

consequently, as knowledge currently stands, no additional impact on public health is expected for the proprietary medicinal product LYNPARZA (olaparib) in this indication.

Considering all these elements, the Committee deems that the clinical benefit of LYNPARZA (olaparib) is:
- **<u>moderate</u> in the MA subpopulation represented by patients with germline BRCA1/2-mutations who have metastatic adenocarcinoma of the pancreas and have not progressed after a minimum of 16 weeks of platinum treatment within a first-line chemotherapy regimen and who are not suitable for continuation of platinum-based chemotherapy.**
- **<u>insufficient</u> to justify public funding cover in the rest of the MA population: patients suitable for continuation of platinum-based chemotherapy, in the absence of any available specific data.**

The Committee issues a favourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use only in the subpopulation of patients with germline BRCA1/2-mutations who have metastatic adenocarcinoma of the pancreas and have not progressed after a minimum of 16 weeks of platinum treatment within a first-line chemotherapy regimen and who are not suitable for continuation of platinum-based chemotherapy.

The Committee issues an unfavourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the rest of the MA population: patients suitable for continuation of platinum-based chemotherapy, in the absence of any available specific data.

Recommended reimbursement rate: 100%

Clinical Added Value

Considering:

- **demonstration of an increase in median progression-free survival (primary endpoint) of +3.6 months in favour of the olaparib group compared to placebo (7.4 months versus 3.8 months (HR = 0.531 CI95% [0.346; 0.815]) in a randomised double-blind study,**
- **the inadequately met medical need in this cancer with a very poor prognosis,**

but,

- **the absence of demonstration of an increase in overall survival, a ranked secondary endpoint (median overall survival between the olaparib group and the placebo group: 18.9 months versus 18.1 months, HR = 0.906; CI95% [0.563; 1.457]; NS,**
- **the choice of comparator group in the study: absence of treatment (placebo) after a limited number of first-line chemotherapy cycles, highly debatable since, in practice, treatment is continued until disease progression or intolerance,**
- **the choice of primary endpoint (progression-free survival), the clinical relevance of which can be criticised in the context of metastatic pancreatic cancer,**
- **the safety profile of this treatment as maintenance therapy (around one in three patients (39.6%) had grade ≥ 3 adverse events),**

the Committee considers that LYNPARZA (olaparib) provides no clinical added value (CAV V) in the MA subpopulation represented by patients with germline BRCA1/2-mutations who have metastatic adenocarcinoma of the pancreas and have not progressed after a minimum of 16 weeks of platinum treatment within a first-line chemotherapy regimen and who are not suitable for continuation of platinum-based chemotherapy.

In the rest of the MA population, the CAV is not applicable.