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Date of Request: December 22, 2014
NCCN Guidelines Panel: Ovarian Cancer

Dear Sir or Madam:

This letter is a formal request to the National Comprehensive Cancer Network (NCCN) Panel for review of data for LYNPARZA® (olaparib) in the treatment of relapsed ovarian cancer. Lynparza is a poly (ADP-ribose) polymerase (PARP) inhibitor.

These materials may include information that is not found in the currently approved prescribing information for Lynparza. The enclosed information is intended to provide pertinent data and should in no way be construed as a recommendation for the use of this product in any manner other than as approved by the Food and Drug Administration and as described in the prescribing information for Lynparza.

The rationale for the recommended change is to provide health care professionals with information regarding the efficacy and safety of Lynparza that have been evaluated in clinical trials.

Specific Changes: Recommend inclusion of Lynparza as an acceptable targeted recurrence therapy as a single agent maintenance therapy in platinum sensitive patients in response to their last platinum therapy and as an acceptable single agent targeted therapy in patients having received at least three prior lines of chemotherapy. Both recommendations require patients to be positive for a deleterious or suspected deleterious germline BRCA (gBRCA)-mutation.

FDA Status: Lynparza was approved by FDA on December 19, 2014. The indication is as monotherapy in patients with deleterious or suspected deleterious germline *BRCA* mutated (as detected by an FDA-approved test) advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy

Rationale: The first five citations describe use of Lynparza as a treatment for advanced cancer which formed the basis for FDA approval as a treatment for gBRCA mutation positive ovarian cancer. The last two citations describe analyses of a randomized, double-blind, placebo-controlled trial that evaluated Lynparza versus placebo following response after platinum-based chemotherapy in patients with platinum-sensitive relapsed high grade serous Ovarian Cancer.

The following articles are submitted in support of this proposal. We would like to acknowledge the contributions of NCCN panel members who are also co-authors or co-contributors of some of these publications.

1. Kaufman B, et al. Olaparib Monotherapy in Patients With Advanced Cancer and a Germline BRCA1/2 Mutation. J Clin Oncol. 2014 Nov 3. pii: JCO.2014.56.2728.
2. Fong P et al. Poly(ADP)-Ribose Polymerase Inhibition: Frequent Durable Responses in BRCA Carrier Ovarian Cancer Correlating With Platinum-Free Interval. J Clin Oncol 2010; 28: 2512-2519.
3. Audeh W et al. Oral poly(ADP-ribose) polymerase inhibitor olaparib in patients with BRCA1 or BRCA2 mutations and recurrent ovarian cancer: a proof-of-concept trial. Lancet 2010; 376: 245–51.
4. Gelmon K et al. Olaparib in patients with recurrent high-grade serous or poorly differentiated ovarian carcinoma or triple-negative breast cancer: a phase 2, multicentre, open-label, non-randomised study. Lancet Oncol 2011; 12: 852–61.
5. Kaye S et al. Phase II, Open-Label, Randomized, Multicenter Study Comparing the Efficacy and Safety of Olaparib, a Poly (ADP-Ribose) Polymerase Inhibitor, and Pegylated Liposomal Doxorubicin in Patients With *BRCA1* or *BRCA2* Mutations and Recurrent Ovarian Cancer. J Clin Oncol 2012; 30:372-379.
6. Ledermann, J et al. Olaparib Maintenance Therapy in Platinum-Sensitive Relapsed Ovarian Cancer. N Engl J Med 2012; 366:1382-1392 .
7. Ledermann J et al. Olaparib maintenance therapy in patients with platinum-sensitive relapsed serous ovarian cancer: a pre-planned retrospective analysis of outcomes by BRCA status in a randomised phase 2 trial. Lancet Oncol 2014;15:852–861.

Sincerely,

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