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NCCN Guidelines Panel: Breast Cancer

On behalf of Pfizer Oncology, I respectfully request the NCCN Breast Cancer Guideline Panel to review the enclosed information for inclusion of TALZENNA™ (talazoparib) as a treatment option for adult patients with deleterious or suspected deleterious germline BRCA-mutated (*gBRCAm*) human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer. TALZENNA (talazoparib) is an inhibitor of poly (ADP-ribose) polymerase (PARP) enzymes, including PARP1 and PARP2, which play a role in DNA repair.

Specific Changes: Recommend the addition of TALZENNA (talazoparib) for the treatment of adult patients with deleterious or suspected deleterious *gBRCAm* HER2-negative locally advanced or metastatic breast cancer.

FDA Clearance: On October 16th, 2018, FDA approved TALZENNA (talazoparib), a PARP inhibitor, for the treatment of adults with deleterious or suspected deleterious *gBRCAm* HER2-negative locally advanced or metastatic breast cancer.

Rationale: The proposed change is based on the FDA-approved indication and data from EMBRACA trial (NCT01945775), TALZENNA (talazoparib) demonstrated significantly longer progression-free survival than physician's choice chemotherapy in adult patients with *gBRCAm* HER2-negative locally advanced or metastatic breast cancer.
EMBRACA was a Phase 3, randomized, open-label study in which patients with advanced breast cancer and a germline BRCA1/2 mutation were assigned, in a 2:1 ratio, to receive talazoparib (1 mg once daily) or standard single-agent physician's choice chemotherapy (capecitabine, eribulin, gemcitabine, or vinorelbine in continuous 21-day cycles).

The trial enrolled 431 patients; 287 were assigned to receive talazoparib and 144 were assigned to receive standard chemotherapy. The primary end point was progression-free survival (PFS), which was assessed by blinded independent central review. Median PFS in the talazoparib group was 8.6 months (95% CI: 7.2 to 9.3) compared to 5.6 months (95% CI: 4.2 to 6.7) in the standard-therapy group (hazard ratio for disease progression or death: 0.54; 95% CI: 0.41 to 0.71; P<0.001). Objective response rate in the talazoparib arm was 62.6% vs. 27.2% in the control arm (odds ratio, 5.0; 95% CI, 2.9 to 8.8; P<0.001). Overall survival results are immature at this time.

The most common adverse events (all grades; ≥ 20%) in the TALZENNA (talazoparib) arm were anemia, fatigue, nausea, neutropenia, headache, thrombocytopenia, alopecia, vomiting, diarrhea, and decreased appetite. The most frequently reported Grade ≥3 adverse reactions (≥5%) for TALZENNA (talazoparib) were anemia, neutropenia, and thrombocytopenia. The incidence of serious AEs was 31.8% in the talazoparib arm and 29.4% in the chemotherapy arm. Adverse events resulting in discontinuation of the drug occurred in 5.9% of talazoparib patients and in 8.7% of chemotherapy patients.

Patient-reported outcomes showed a significant overall improvement from baseline in global health status−quality-of-life with talazoparib (3.0 (95% CI: 1.2 to 4.8)) in comparison with physician's choice therapy, which showed a significant deterioration (−5.4 (95% CI: −8.8 to −2.0)) (P<0.0001). Significant

delays in the time to clinically meaningful deterioration according to both the global health status-quality-of-life and breast symptoms scales were observed in the talazoparib arm as compared with a nonsignificant change in the chemotherapy arm.

The following references are submitted in support of this proposed change.

1. TALZENNA (talazoparib) Prescribing Information. Pfizer , Inc.


Talazoparib Prescribing Informati

2. Litton JK, Rugo HS, Ettl J, et al. Talazoparib in Patients with Advanced Breast Cancer and a Germline BRCA Mutation. N Engl J Med. 2018;379(8):753-763.


Litton et al_NEJM-2018.pdf


Litton et al_NEJM-2018_suppl

3. Ettl J, Quek RGW, Lee K-H, et al. Quality of life with talazoparib versus physician's choice of chemotherapy in patients with advanced breast cancer and germline *BRCA1/2* mutation: patient-reported outcomes from the EMBRACA phase III trial. Ann Oncol. 2018 Aug 15. doi: 10.1093/annonc/mdy257. [Epub ahead of print].


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We appreciate the Panel's thorough consideration of Pfizer's recommendation that TALZENNA (talazoparib) be added for the treatment of adults with *gBRCAm* HER2-negative locally advanced or metastatic breast cancer. We welcome any questions that you may have.

Kind regards,
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