Submitted by: Chief Medical Officer
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NCCN Guidelines Panel: Genetic/Familial High Risk Assessment: Breast and Ovarian

Specific Changes:

Change top line of page BRCA-1 from **"BRCA1/2 testing criteria"** to **"BRCA1/2 and PALB2 testing criteria"**.

FDA Clearance: Not applicable

Rationale:

With the advent of panel testing, other genes with risk for breast and ovarian cancer are regularly included along with testing of *BRCA1/2*. ***PALB2* has been consistently shown to confer a breast cancer risk similar in magnitude to *BRCA2*.** As such, risk reducing mastectomy may be an appropriate intervention for patients with a pathogenic variant in *PALB2*. When a risk-reducing surgical option is available, the implications to patient management are important enough that, given risks similar to *BRCA2*, this gene should be highlighted in the testing criteria.

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

Antoniou AC, Casadei S, Heikkinen T et al. Breast-cancer risk in families with mutations in PALB2. N Engl J Med. 2014 Aug 7;371(6):497-506.

Kurian AW, Hughes E, Handorf EA, et. al. Breast and Ovarian Cancer Penetrance Estimates Derived From Germline Multiple-Gene Sequencing Results in Women. JCO Precision Oncology 2017.

Easton DF, Pharoah DP, Antoniou AC, et al. Gene-panel sequencing and the prediction of breast-cancer risk. N Engl J Med. 2015 372: 2243-2257.

Sincerely,

Johnathan Lancaster, MD, PhD
Chief Medical Officer
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