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NCCN Guidelines Panel: Genetic/Familial High Risk Assessment: Breast and Ovarian

Specific Changes: Provide specific testing criteria, as well as management recommendations, for PALB2 analogous to the testing criteria and recommendations provided for BRCA1/2, PHTS, LFS, and the other genes/syndromes addressed in the guidelines.

FDA Clearance: Not applicable.

Rationale: Multiple studies have demonstrated that the female breast cancer risk associated with pathogenic variants in PALB2 is similar to that for BRCA2, and this level of risk is high enough to justify consideration of breast cancer risk reduction measures similar to the recommendations for women with pathogenic variants detected in BRCA1/2. Depending on the study population and mutation detection strategy utilized, 0.4% to 4.5% of women ascertained for BRCA1/2 testing have been found to carry pathogenic variants in PALB2, demonstrating that this gene is a significant contributor to hereditary female breast cancer risk, as well as pancreatic cancer, and possibly male breast cancer and ovarian cancer.

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


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Sincerely,

[Signature]

Johnathan Lancaster, MD, PhD
Chief Medical Officer
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