Specific Changes: Provide specific testing criteria, as well as management recommendations, for \textit{PALB2} analogous to the testing criteria and recommendations provided for \textit{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 \textit{PALB2} is similar to that for \textit{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 \textit{BRCA1/2}. Depending on the study population and mutation detection strategy utilized, 0.4\% to 4.5\% of women ascertained for \textit{BRCA1/2} testing have been found to carry pathogenic variants in \textit{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.


Sincerely,

[Signature]

Johnathan Lancaster, MD, PhD
Chief Medical Officer
Myriad Genetic Laboratories Inc.