Specific Changes: On page GENE-1, delete bullet point 7 (regarding moderate penetrance genes) and modify bullet point 2 as follows:

- The majority of patients meeting assessment and testing criteria for inherited breast and/or ovarian cancer risk have personal and/or family histories that can be explained by multiple genes or syndromes, and are therefore most appropriately tested with a multi-gene panel. A small subset of patients with a personal or family history narrowly suggestive of a single syndrome with highly distinctive features (e.g., Peutz-Jeghers Syndrome or Neurofibromatosis I) may be most appropriately managed by genetic testing for that specific syndrome.

FDA Clearance: Not applicable.

Rationale: In the past few years, multiple studies in varied populations of women at risk for hereditary breast, ovarian and other cancers have demonstrated that multi-gene/syndrome panels result in a significant increase in the identification of individuals who can benefit from substantive medical management interventions compared to testing for single genes/syndromes or family history analysis. Among women meeting current NCCN criteria for BRCA1/2 testing, there are no criteria by which it is possible to reliably determine who is more or less likely to benefit from testing with a panel including most of the genes listed in the table on pages GENE-2 to GENE-4, and there is evidence that panel test findings, including those in moderate penetrance genes, frequently result in medical management recommendations that would not have been identified by family history analysis alone.

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,

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