



Submitted by: Chief Medical Officer  
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NCCN Guidelines Panel: Uterine Neoplasms

Specific Changes: Add a footnote on page UN-1 clarifying the final “Initial Evaluation” bullet point about genetic counseling/testing for patients with a significant family history of endometrial and/or colorectal cancer. Specifically, the footnote could state:

- Consider genetic testing for patients with endometrial cancer <50 years, a family history that meets the Revised Bethesda or Amsterdam criteria and/or individuals with a  $\geq 5\%$  risk of Lynch Syndrome on an accepted mutation prediction model such as MMRpro, PREMM(1,2,6) or MMRpredict.

FDA Clearance: Not applicable.

Rationale: Women with Lynch syndrome present with gynecological cancer as their first cancer approximately 50% of the time, and these patients have substantial risk for a second primary cancer after an endometrial cancer. Therefore, it is critical that health providers who manage patients with uterine cancer identify this high risk group. This request is in alignment with the Lynch Syndrome testing criteria on page LS-1 in the Genetic/Familial High-Risk Assessment: Colorectal NCCN guidelines. Having this additional detail replicated in the Uterine Neoplasms guideline makes it easier for treating physicians to easily identify appropriate patients, as opposed to suggesting that they should reference a separate guideline in order to know who is appropriate for further assessment.

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.

Provenzale D et al. NCCN Clinical Practice Guidelines in Oncology®: Genetic/Familial High-Risk Assessment: Colorectal. V 2.2015. October 7. Available at <http://www.nccn.org>.

Lu K et al, Gynecological cancer as a “sentinel cancer” for women with hereditary non-polyposis colorectal cancer syndrome. Obstet Gyn 2005; 105(3):569-74.

Win A, et al, Risk of colorectal and other cancers after endometrial cancer in women with Lynch syndrome. JNCI 2013; 105(4):274-279.

Kastrinos F et al. The PREMM(1,2,6) model predicts risk of MLH1, MSH2, and MSH6 germline mutations based on cancer history. Gastroenterology 2011; 140(1):73-81.

Sincerely,

A handwritten signature in black ink, appearing to be 'J. Lancaster', with a stylized, cursive script.

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