



Submitted by: Chief Medical Officer
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Date of request: October 8th, 2015
NCCN Guidelines Panel: Genetic/Familial High –Risk Assessment: Colorectal

Specific Changes: Recommend consideration of a multi-syndrome gene panel for patients meeting clinical testing criteria for a hereditary colon cancer syndrome.

FDA Clearance: Not applicable.

Rationale: Tumor testing is not always available for patients with a past cancer diagnosis or patients in the community setting. Furthermore, multiple studies have demonstrated that multi-syndrome panel testing significantly increases the number of individuals identified with clinically significant pathogenic variants for which there are guideline-supported medical management interventions. Challenges to single syndrome testing include syndrome overlap (e.g. *BRCA1* or *BRCA2* mutations in families with apparent Lynch syndrome), potential delay and expense incurred undergoing sequential testing for multiple syndromes, and complicated or limited family histories.

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.

Gallego CJ, Shirts BH, Bennette CS, Guzauskas G, Amendola LM, Horike-Pyne M, Hisama FM, Pritchard CC, Grady WM, Burke W, Jarvik GP, Veenstra DL. Next-Generation Sequencing Panels for the Diagnosis of Colorectal Cancer and Polyposis Syndromes: A Cost-Effectiveness Analysis. J Clin Oncol. 2015 Jun 20;33(18):2084-91.

Yurgelun MB, Allen B, Kaldete RR, Bowles KR, Judkins T, Kaushik P, Roa BB, Wenstrup RJ, Hartman AR, Syngal S. Identification of a Variety of Mutations in Cancer Predisposition Genes in Patients With Suspected Lynch Syndrome. Gastroenterology. 2015 Sep;149(3):604-613.

LaDuca H, Stuenkel AJ, Dolinsky JS, Keiles S, Tandy S, Pesaran T, Chen E, Gau CL, Palmaer E, Shoaepour K, Shah D, Speare V, Gandomi S, Chao E. Utilization of multigene panels in hereditary cancer predisposition testing: analysis of more than 2,000 patients. Genet Med. 2014 Nov;16(11):830-7.

Chubb D, Broderick P, Frampton M, Kinnersley B, Sherborne A, Penegar S, Lloyd A, Ma YP, Dobbins SE, Houlston RS. Genetic diagnosis of high-penetrance susceptibility for colorectal cancer (CRC) is achievable for a high proportion of familial CRC by exome sequencing. J Clin Oncol. 2015 Feb 10;33(5):426-32.

Yurgelun MB, Masciari S, Joshi VA, Mercado RC, Lindor NM, Gallinger S, Hopper JL, Jenkins MA, Buchanan DD, Newcomb PA, Potter JD, Haile RW¹, Kucherlapati R¹, Syngal S¹; Colon Cancer Family Registry. Germline TP53 Mutations in Patients With Early-Onset Colorectal Cancer in the Colon Cancer Family Registry. JAMA Oncol. 2015 May;1(2):214-21.

Sincerely,

A handwritten signature in black ink, appearing to be 'JL' with a large loop and a trailing flourish.

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