



Submitted by: Medical Director, Dermatology
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NCCN Guidelines Panel: Melanoma

Specific Changes: Adjust current content regarding genetic testing for inherited melanoma risk to improve consistency and provide additional clinical relevance:

- 1) On pages ME-A-1 and ME-11, use the same list of relevant genes: *CDKN2A*, *CDK4*, *BAP1*, *TERT*, *MITF*, *MC1R*.
- 2) On page ME-A-1 and ME-11, use the same list of relevant malignancies suggestive of inherited risk: cutaneous and uveal melanoma, pancreatic cancer, astrocytoma, mesothelioma and kidney.
- 3) Add additional content to the last bullet point on page ME-11 regarding the importance of genetic testing: "Identification of a germline mutation in a melanoma patient can provide important information about risk for additional primary melanomas, as well as the risk for other cancers. This information can guide management recommendations for prevention and early detection in the patient and relatives."
- 4) Adjust the wording in the last bullet point on page ME-11 from "Consider referral to a genetic counselor...." To "Consider genetic counseling...."
- 5) Add Leachman et al. (citation 1 below) to the references for genetic testing, as this is a recent, comprehensive discussion of hereditary risk for melanoma.

FDA Clearance: Not applicable.

Rationale: The current guidelines have discrepancies in the genes mentioned as testing targets and relevant cancers for risk assessment in different places. Resolving these discrepancies will increase the utility of the guidelines. Kidney cancer is an associated cancer for *BAP1* and *MITF*. Additionally, clinicians may benefit from more explicit statements regarding the clinical utility of the testing – in this context it is useful to note the studies demonstrating that genetic test results can have a significant impact on compliance with screening and sun protective behavior in families with hereditary melanoma. Lastly, as outlined in the most recent ASCO position statement on cancer genetic testing, genetic counseling is a process that can be provided by any appropriately trained physician, including dermatologists, and should not be restricted to genetic counselors.

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:

1. Leachman SA, et al. Identification, genetic testing, and management of hereditary melanoma. *Cancer Metastasis Rev.* 2017 Mar;36(1):77-90. PMID: 28283772.
2. Aspinwall LG, et al. Genetic test reporting of CDKN2A provides informational and motivational benefits for managing melanoma risk. *Transl Behav Med.* 2018 Jan 29;8(1):29-43. PMID:29385581.
3. Wu YP, et al. A novel educational intervention targeting melanoma risk and prevention knowledge among children with a familial risk for melanoma. *Patient Educ Couns.* 2018 Mar;101(3):452-459. PMID: 29078964.
4. Stump TK, et al. Genetic Test Reporting and Counseling for Melanoma Risk in Minors May Improve Sun Protection Without Inducing Distress. *J Genet Couns.* 2018 Aug;27(4):955-967. PMID: 29349527.
5. Robson ME, et al. American Society of Clinical Oncology Policy Statement Update: Genetic and Genomic Testing for Cancer Susceptibility. *J Clin Oncol.* 2015 Nov 1;33(31):3660-7. PMID: 26324357.

Sincerely,

A handwritten signature in cursive script that reads "Loren Clarke". The signature is written in black ink and is positioned below the word "Sincerely,".

Loren Clarke, MD
Medical Director, Dermatology, Myriad Genetic Laboratories Inc.