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NCCN Guidelines Panel:	Melanoma

Specific Changes: Incorporate a recommendation for genetic risk assessment/testing for individuals meeting specified personal and family history criteria to the Initial Clinical Assessment algorithm for newly diagnosed patients (page ME-1) and as part of the discussion of risk factors (page MS-2).

FDA Clearance: Not applicable.

Rationale: It is estimated that 10% of melanomas are due to inherited mutations in melanoma susceptibility genes and criteria for genetic counseling/testing relevant to melanoma patients are available from the American College of Medical Genetics and the International Melanoma Genetics Consortium. Using criteria of 3 or more melanomas diagnosed in an individual or family, or a mix of melanoma and pancreatic cancer diagnoses in a single individual or close relatives, up to 41% of individuals are positive for pathogenic variants in the genes *CDKN2A* and *CDK4*. It may be appropriate to reduce the criteria to 2 cases of melanoma and/or pancreatic cancer in an individual or family, especially in areas of lower melanoma incidence. Providing specific language around the type of personal/family history warranting genetic risk assessment for melanoma patients facilitates the ascertainment of appropriate candidates for genetic testing to identify cancer risks relevant to their own care and the care of their relatives.

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. Hampel H, et al. A practice guideline from the American College of Medical Genetics and Genomics and the National Society of Genetic Counselors: referral indications for cancer predisposition assessment. *Genet Med*. 2015 17:70-87. PMID:25394175.

2. Goldstein AM, et al. High-risk melanoma susceptibility genes and pancreatic cancer, neural system tumors, and uveal melanoma across GenoMEL. Cancer Res. 2006 66:9818-28. PMID: 17047042.

3. Leachman SA, et al. Selection criteria for genetic assessment of patients with familial melanoma. J Am Acad Dermatol. 2009 61:677.e1-14. PMID: 19751883.

4. Ransohoff KJ, et al. Familial skin cancer syndromes: Increased melanoma risk. *J Am Acad Dermatol*. 2016 74:423-34. PMID: 26892652.

5. Soura E, et al. Hereditary melanoma: Update on syndromes and management: Emerging melanoma cancer complexes and genetic counseling. *J Am Acad Dermatol.* 2016 74:411-20. PMID:26892651.

6. Soura E, et al. Hereditary melanoma: Update on syndromes and management: Genetics of familial atypical multiple mole melanoma syndrome. J Am Acad Dermatol. 2016 74:395-407. PMID:26892650.

Sincerely,

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