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Corporate Medical Policy

Genetic Testing for Familial Cutaneous Malignant Melanoma AHS – M2037

File Name:	genetic_testing_for_familial_cutaneous_malignant_melanoma
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Description of Procedure or Service

Description

Skin cancer is the most common form of cancer, arising from the metaplastic transformation from any of the cell types of the skin (Linares, Zakaria, & Nizran, 2015). Melanomas, which develop from the pigment-producing melanocytes, although much less prevalent than non-melanoma skin cancer, are increasing in incidence (Holmes, 2014; Lee & Lian, 2018). Early and accurate diagnosis is essential, as late-stage melanoma is among the most fatal forms of skin cancer (Cockerell et al., 2017). This, however, presents a significant challenge due to the difficulty of interpreting the histopathology of melanoma and the resulting interobserver and intra-observer variability (Elmore et al., 2017; Gerami et al., 2014).

This policy covers testing to assess the genetic risk of familial cutaneous melanoma and diagnostic testing to differentiate melanocytic lesions with indeterminate histopathology. Genetic testing of melanoma tumors for therapy is addressed in M2109 Molecular Panel Testing of Cancers for Diagnosis, Prognosis, and Identification of Targeted Therapy and M2029 Genetic Testing and Genetic Expression Profiling in Patients with Cutaneous Melanoma.

Related Policies

Genetic Testing and Genetic Expression Profiling in Patients with Cutaneous Melanoma AHS – M2029
Molecular Panel Testing of Cancers for Diagnosis, Prognosis, and Identification of Targeted Therapy AHS – M2109

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

Genetic testing for familial cutaneous malignant melanoma is considered investigational. BCBSNC does not provide coverage for investigational services or procedures.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

Genetic Testing for Familial Cutaneous Malignant Melanoma AHS – M2037

When Genetic Testing for Familial Cutaneous Malignant Melanoma is covered

Not applicable.

When Genetic Testing for Familial Cutaneous Malignant Melanoma is not covered

Genetic testing for inherited forms of melanoma is considered investigational.

Policy Guidelines

Background

Cutaneous melanoma is one of the most aggressive forms of skin cancer due to its potential for metastasis with poor prognosis when not detected and treated at early stages (Leonardi et al., 2018; Soura, Eliades, Shannon, Stratigos, & Tsao, 2016b). Unlike other solid tumors, melanoma affects young and middle-aged individuals with a median age at diagnosis of 57 (Leonardi et al., 2018). Melanoma incidence and mortality are on the rise (Chiaravalloti, Jinna, Kerr, Whalen, & Grant-Kels, 2018; Siegel, Miller, & Jemal, 2017), with the lifetime risk of developing cutaneous melanoma estimated to be 1 in 34 for women and 1 in 53 for men (Siegel et al., 2017).

Ultraviolet (UV) light radiation from sun exposure is a major risk factor for melanoma skin cancer development (Gilchrest, Eller, Geller, & Yaar, 1999; Holmes, 2014), directly associated with an increased risk of melanoma (Leonardi et al., 2018; Pennello, Devesa, & Gail, 2000). Skin type, number of congenital and acquired melanocytic nevi, genetic susceptibility, and a family history have also been associated with increased risk for melanoma (Bauer & Garbe, 2003; Bevona, Goggins, Quinn, Fullerton, & Tsao, 2003; Hawkes, Truong, & Meyer, 2016). In addition to the total number of nevi, the size and type of nevi are also individually associated with an increased risk of melanoma, as approximately 25% of melanomas originate from an existing nevus (Gandini et al., 2005; Watt, Kotsis, & Chung, 2004). Interestingly, a greater number of nevi with a 3mm diameter or larger was recently associated with melanoma death in males but not in females (Li et al., 2019). Early and accurate identification of patients with increased risk of melanoma development is essential to enable risk-tailored surveillance, management of early staged patients with biologically aggressive tumors (Zager et al., 2018), and improvement of patient outcomes (Cockerell et al., 2017).

Genetic Testing for Familial Cutaneous Melanoma

A family history of melanoma is reported by about 10% of melanoma patients (Soura et al., 2016b), and inherited germline mutations reportedly "increase melanoma risk from 4- to >1000-fold" (Ransohoff et al., 2016). Determining the genetic origin, however, is complicated, as a portion of familial melanoma can be attributed to shared sun exposure experiences in family members with susceptible skin types (Goldstein & Tucker, 2001). The majority of familial cases lack identifiable germ-line mutations in either kno43wn susceptibility genes or in genes commonly mutated in sporadic melanoma (Hawkes et al., 2016). Uncommon, but high-risk, alleles have been found to contribute to the hereditary cancer phenotype that includes unilateral lineage, multi-generational, multiple primary lesions, and early onset of disease (Soura et al., 2016b). Additional research has identified a relationship between telomere length and familial melanoma; patients with familial melanoma had longer telomeres compared to patients with sporadic melanoma (Menin et al., 2016).

Cyclin-dependent kinase inhibitor 2A (*CDKN2A*) and cyclin-dependent kinase 4 (*CDK4*) are the most commonly identified gene mutations in familial forms of melanoma. Germline *CDKN2A* mutations have been identified in approximately 40% of familial melanoma cases where three or more family members are affected (Harland et al., 2016). *CDKN2A* encodes several proteins involved in cell cycle regulation, including p16, which inhibits *CDK4* (Hussussian et al., 1994; Koh, Enders, Dynlacht, & Harlow, 1995), and p14ARF, which inhibits *MDM2* from regulating p53 (Zhang, Xiong, & Yarbrough, 1998). Germline *CDKN2A* mutations in melanoma families are usually missense or nonsense changes that impair the function of the p16 protein, allowing for unchecked cell cycle progression; however, rare mutations in the p14ARF protein have also been reported and result in proteasomal degradation of p53 with subsequent accumulation of DNA damage (Marzuka-Alcala, Gabree, & Tsao, 2014). Overall survival is worse in those with a germline *CDKN2A* mutation than those with sporadic melanoma or familial melanoma with wild-type *CDKN2A* genes. Germline mutations also predisposed patients to an increased number of malignancies, such as pancreatic and lung cancer (Tsao & McCormick, 2020).

Mutations in *CDKN2A*/p16 are associated with familial atypical multiple mole-melanoma (FAMMM syndrome), which is characterized by numerous nevi (some atypical), a family history of melanoma, and an increased risk of pancreatic cancer (Goldstein et al., 2007; Lynch & Krush, 1968). Carriers of a FAMMM mutation typically present with cancer at a younger age than non-carriers (Middlebrooks et al., 2019). Mutations in p14ARF are linked to Melanoma-Astrocytoma Syndrome (MAS), a variant of FAMMM characterized by both cutaneous melanomas and nervous system tumors (Randerson-Moor et al., 2001). Inheritance of *CDKN2A* mutations are autosomal dominant, but these mutations have variable penetrance based on sun exposure patterns and coinheritance of other melanoma-associated variants, conferring a 76% lifetime risk of developing melanoma in the US (Bishop et al., 2002; Cust et al., 2011). Mutations in *CDK4* are even less common, but were most often found affecting arginine 24, resulting in a CDK4 protein that is insensitive to inhibition by the p16 protein. No apparent differences exist in the phenotype (e.g., age at diagnosis, number of melanomas) of families carrying either *CDKN2A* or *CDK4* mutations. In aggregate, between 20-45% of familial melanomas are associated with germline mutations in *CDKN2A* or *CDK4* (Goldstein et al., 2007; Nelson & Tsao, 2009).

Other rare mutations have been associated with melanoma. Germline variations in the melanocortin-1 receptor (*MC1R*) gene alter the risk of melanoma in individuals with and without *CDKN2A* mutations (Marzuka-Alcala et al., 2014; Pasquali et al., 2015; Wendt et al., 2018). Germline variants in genes that encode for *BRCA1*-associated protein-1 (*BAP1*), telomerase reverse transcriptase (*TERT*), and microphthalmia-associated transcription factor (*MITF*) have also been added to the list of genes harboring familial melanoma-predisposing mutations (Simone, Valiante, & Silipo, 2017; Soura, Eliades, Shannon, Stratigos, & Tsao, 2016a). These are more often associated with "mixed cancer syndrome," where melanoma may appear in the context of a more general predisposition for malignancy. The *BAP1* tumor syndrome is associated with the appearance of cutaneous melanoma, uveal melanoma, and various internal malignancies (Wiesner et al., 2011). Mutations in the promoter region of *TERT*, the protein component of telomerase, and in various components of the shelterin complex have been associated with a higher incidence of melanoma and other internal malignancies (Burke et al., 2013; Horn et al., 2013). Mutations in *MITF* are associated with a higher nevus count, cutaneous malignant melanoma onset before 40 years of age, and non-blue eye color with no association to freckling, skin color, or hair color (Bertolotto et al., 2011; Yokoyama et al., 2011). X Xeroderma pigmentosum (XP) is a rare disorder in which patients have a mutation in genes involved in nucleotide excision repair (NER). Patients with mutations in *XPC* and *XPD* have an increased risk of melanoma (Paszkowska-Szczur et al., 2013). Lastly, Cowden syndrome, a type of *PTEN* hamartoma tumor syndrome characterized by the appearance of trichilemmomas, papillomatous papules, mucosal lesions (papules) and palmar-plantar keratosis within the first three decades of life, is associated with a higher risk of melanoma (Bubien et al., 2013; Soura et al., 2016a).

Several proprietary gene panels exist for assessment of familial cutaneous melanoma. For example, Invitae offers a 12-gene panel (9 primary genes plus 3 genes with "preliminary evidence for melanoma"), Fulgent offers a 14-gene panel, and GeneDx offers a 9-gene panel (Fulgent, 2020; GeneDx, 2020; Invitae, 2020). These panels may include genes traditionally associated with familial melanoma itself (such as *CDKN2A*) as well as genes whose variants are not primarily associated with familial melanoma, but confer added risk regardless (Tsao & McCormick, 2020).

Clinical Utility and Validity of Genetic Testing for Familial Cutaneous Melanoma

The frequency of *CDKN2A* mutations in patients with a single primary melanoma or multiple primary melanoma were 1.2% and 2.9%, respectively (Berwick et al., 2006); however, depending on selection criteria, mutation frequency rates of *CDKN2A* can range from 5% to 72% (Delaunay et al., 2017) with a family history of melanoma considered the most important risk factor. The established rule of three is used when proposing genetic testing for primary melanomas; it is generally understood that when three or more melanomas or genetically related cancers are identified in the same patient, or in first- and second-degree relatives, the pretest probability is increased above 10% and the cost of genetic screening can be justified (Leachman et al., 2017).

Potjer et al. (2019) have determined that "Germline mutations in the major melanoma susceptibility gene *CDKN2A* explain genetic predisposition in only 10-40% of melanoma-prone families" and subsequently characterized 488 melanoma cases from non-*CDKN2A*/*CDK4* families to determine other important mutations in familial melanoma. The authors conclude that "multigene panel testing for familial melanoma is appropriate considering the additional 4% diagnostic yield in non-*CDKN2A*/*CDK4* families. Our study shows that *BAP1* and *MITF* are important genes to be included in such a diagnostic test (Potjer et al., 2019)."

Stolarova et al. (2020) analyzed 264 Czech melanoma patients with early onset, double primary tumors or family history by next generation sequencing NGS analysis of 217 genes, and they identified that "mutations in high-to-moderate melanoma risk genes and in other cancer syndrome genes were significantly associated with melanoma risk," with those genes including *CDKN2A, POT1,* and *ACD* for high-to-moderate melanoma risk, and *NBN, BRCA1/2, CHEK2, ATM, WRN,* and *RB1* for other cancer syndrome genes. An increased potential of carrying mutations was found in "patients with double primary melanoma, melanoma and other primary cancer, but not in patients with early age at onset" (Stolarova et al., 2020). *CDK2NA* was the most frequently mutated gene among those with high-to-moderate risk, and in other studies reviewed by Stolarova et al. (2020), there was an increased risk for pancreatic cancer among families with *CDK2NA* mutation, and a more established family history.

Leachman et al. (2017) published an updated algorithm for the identification, testing, and management of hereditary melanoma; the rule of three has been incorporated into this algorithm as an indication for genetic testing in multiple melanomas. The researchers state that "Any patient or family that meets the updated rule of threes should be considered a candidate for genetic testing. If melanoma is the only cancer in a pedigree, then to meet the threshold of genetic testing, a pedigree should have three primary melanomas in first- or second-degree relatives in areas with a high melanoma incidence or two primary melanomas in a low-incidence area. This melanoma panel should include *BAP1*, *CDK4*, and *CDKN2A*. Genes for which risk has not been established but for which studies suggest an elevated risk include *MITF* and *POT1* and we recommend including these in the melanoma panel" (Leachman et al., 2017).

The clinical utility of genetic testing for hereditary melanoma families is debatable because *CDKN2A* status may not impact medical management in patients with melanoma (Gabree, Patel, & Rodgers, 2014). This was further confirmed by Tovar-Parra, Gutiérrez-Castañeda, Gil-Quiñones, Nova, and Pulido (2020), who found that *CDKN2A* polymorphisms p.G101W, p.R24P,

p.M53I, and A148T, in a case-control study with 85 cases and 166 controls, were not associated with increased susceptibility to melanoma in the Colombian population, thereby demonstrating the lack of procedures that would need to be taken for those with this mutation. However, testing for *CDKN2A* mutations with genetic counseling was shown to be perceived as more informative and motivating to patients to adhere to prevention recommendations (Aspinwall et al., 2018). Compared to no-test controls, participants who received test results (carriers and noncarriers) reported feeling significantly more informed and prepared to manage their risk, and carriers reported greater motivation to reduce sun exposure; all groups reported low negative emotions about melanoma risk (Aspinwall et al., 2018). Parents reported high levels of preparedness to manage children's risk regardless of group. Carrier parents reported greater (but moderate) worry about their children's risk than no-test control parents.

Genetic testing for commonly known cutaneous melanoma mutations can be utilized to determine prognosis and overall survival. Aoude et al. (2020) found that "germline mutation status was the most significant biomarker for OS [overall survival]" and "survival outcomes for germline carriers are poor with the current standards of care." When using BRAF status and tumor mutation burden (TMB) for prognosis of cutaneous melanoma patients, "BRAF V600 wild-type patients had significantly longer PFS [progression-free survival] than the V600 mutant group ($p = 0.0317$) … For stage III/IV resected patients, TMB was also significantly associated with longer PFS ($p = 0.0034$)" (Aoude et al., 2020). The greater the number of recognizable mutations, the more targeted attacks against cancerous cells can be made and the better the prognosis.

Guidelines and Recommendations

National Comprehensive Cancer Network (NCCN, 2020)

The NCCN Guidelines for Cutaneous Melanoma recommend to "Consider the use of molecular testing for histologically equivocal lesions," either with comparative genomic hybridization (CGH) or fluorescence *in situ* hybridization (FISH) for detecting genetic mutations. The NCCN also states, "Prognostic gene expression profiling (GEP) to differentiate melanomas at low versus high risk for metastasis may provide information on individual risk of recurrence, as an adjunct to standard AJCC staging. However, the currently available prognostic molecular techniques should not replace pathologic staging procedures, and the use of GEP testing according to specific melanoma stage (before or after SLNB [sentinel lymph node biopsy]) requires further prospective investigation in large, contemporary data sets of unselected patients" (NCCN, 2020).

On testing of primary lesions, the NCCN recommends that "mutational analysis for *BRAF* or multigene testing of the primary lesion is not recommended for patients with cutaneous melanoma who are without evidence of disease (NED), unless required to guide adjuvant or other systemic therapy or consideration of clinical trials" (NCCN, 2020).

Further, the NCCN also recommended that a referral should be considered for genetic counseling "for p16/*CDKN2A* mutation testing in the presence of 3 or more invasive cutaneous melanomas, or a mix of invasive melanoma, pancreatic cancer, and/or astrocytoma diagnoses in an individual or family. Testing for other genes that can harbor melanoma-predisposing mutations (e.g., *MC1R, CDK4*, *TERT*, *MITF*, *BRCA2*, and *BAP1*) [especially for a uveal melanoma] may be warranted" (NCCN, 2020).

Indications for genetic testing using emerging molecular technologies for diagnosis and prognostication, the NCCN recommended the following:

- "The panel does not recommend *BRAF* or NGS [next generation sequencing] testing for resected stage I-II cutaneous melanoma unless it will inform clinical trial participation.
- *BRAF* mutation testing is recommended for patients with stage III at high risk for recurrence for whom *BRAF*-directed therapy may be an option.
- For initial presentation with stage IV disease or clinical recurrence, obtain tissue to ascertain alterations in *BRAF*, and in the appropriate clinical setting. *KIT* from either biopsy of the metastasis (preferred) or archival material if the patient is being considered for targeted therapy. Broader genomic profiling (e.g., larger NGS panels, *BRAF* non-V600 mutation) is recommended if feasible, especially if the test results might guide future treatment decisions or eligibility for participation in a clinical trial.
- If *BRAF* single-gene testing was the initial test performed, and is negative, clinicians should strongly consider larger NGS panels to identify other potential genetic targets (e.g., *KIT*, *BRAF* non-V600)" (NCCN, 2020).

The American Academy of Dermatology (AAD) (Swetter et al., 2019)

The AAD recently published guidelines for the care and management of primary cutaneous melanoma. It was stated that "There is insufficient evidence to recommend routine molecular profiling assessment for baseline prognostication. Evidence is lacking that molecular classification should be used to alter patient management outside of current guidelines (eg, NCCN and AAD). The criteria for and the utility of prognostic molecular testing, including GEP, in aiding clinical decision making (e.g., SLNB eligibility, surveillance intensity, and/or therapeutic choice) needs to be evaluated in the context of clinical study or trial (Swetter et al., 2019)." Further, a "C" recommendation was given regarding patient referral for genetic counseling "and possible germline genetic testing for select patients" with potential hereditary cutaneous melanoma (Swetter et al., 2019).

In regards to patients with a family history of invasive cutaneous melanoma (at least three affected members on one side of the family), "Cancer risk counseling by a qualified genetic counselor is recommended" (Swetter et al., 2019).

European Society for Medical Oncology (ESMO) (Michielin, van Akkooi, Ascierto, Dummer, & Keilholz, 2019a)

The ESMO published 2019 guidelines for cutaneous melanoma diagnosis, treatment and follow-up. This article states that "Mutation testing for actionable mutations is mandatory in patients with resectable or unresectable stage III or stage IV [I, A], and is highly recommended in high-risk resected disease stage IIC but not for stage I or stage IIA-IIB. *BRAF* testing is mandatory [I, A] (Michielin, van Akkooi, Ascierto, Dummer, & Keilholz, 2019b)."

Regarding follow-up, long-term implications and survivorship, the ESMO has stated that "Patients must be aware that family members have an increased melanoma risk [III, B]. There is no recommendation for genetic testing" (Michielin et al., 2019b).

European Dermatology Forum (EDF), the European Association of Dermato-Oncology (EADO), and the European Organization for Research and Treatment of Cancer (EORTC) (Garbe et al., 2020)

The EDF, EADO, and EORTC collaboratively released an interdisciplinary guideline on the diagnostics of melanoma. With regards to genetic testing of cutaneous melanoma, the guidelines suggest that genetic profiling of melanoma tissues using NGS may help in identifying the genetic alterations that are targetable by drugs. For specific stages and in relation to the *BRAF* V600 mutation, the guidelines recommend mutation testing for cancers stage III and higher. However, "mutational analysis for *BRAF* of the primary lesion is not recommended for patients with cutaneous melanoma but without evidence of the disease, unless required to guide consideration of clinical trials for adjuvant therapy" (Garbe et al., 2020).

"Mutational analysis is required to determine the BRAFV600 mutation status in patients with distant metastasis or non-resectable regional metastasis to identify those who are eligible to receive treatment with combined BRAF and MEK inhibitors, and in resected high-risk stage III melanoma patients in the adjuvant setting. BRAFV600 mutation testing should be performed on metastatic tissue, either distant or regional, or on primary tumor if sampling of the metastatic tissue is not feasible" (Garbe et al., 2020).

American Joint Committee on Cancer (AJCC) (Gershenwald et al., 2017)

The AJCC did not include any mention of molecular testing in the most recent 8th edition guidance on melanoma staging (Gershenwald et al., 2017).

US Preventive Services Task Force (USPSTF) (Wernli et al., 2016)

The USPSTF examined the utility of visual skin examination for the prevention of melanoma and found that "Only limited evidence was identified for skin cancer screening, particularly regarding potential benefit of skin cancer screening on melanoma mortality" (Wernli et al., 2016). The use of molecular tests in screening for melanoma is not mentioned.

National Cancer Institute (NCI, 2020)

The NCI updated its PDQ cancer information summary on the genetics of skin cancer (NCI, 2002) in June 2018; this was reaffirmed in 2020. It summarizes expert opinion on genetic testing: "Expert opinion regarding testing for germline pathogenic variants of *CDKN2A* follows two divergent schools of thought. Arguments for genetic testing include the value of identifying a cause of disease for the individual tested, the possibility of improved compliance with prevention protocols in individuals with an identified pathogenic variant, and the reassurance of a negative testing result in individuals in a family carrying a pathogenic variant. However, a negative test result in a family that does not have a known pathogenic variant is uninformative; the genetic cause of disease in these patients must still be identified. It should also be noted that members of families carrying a *CDKN2A* pathogenic variant who do not carry the variant themselves may remain at increased risk of melanoma. At this time, identification of a *CDKN2A* pathogenic variant does not affect the clinical management of the affected patient or family members. Close

dermatologic follow-up of these people is indicated, regardless of genetic testing result, and pancreatic cancer screening has unclear utility" (NCI, 2020).

American College of Medical Genetics and Genomics (ACMG) and the National Society of Genetic Counselors (NSGC) (Hampel, Bennett, Buchanan, Pearlman, & Wiesner, 2015)

Referral for cancer genetic consultation is recommended by the ACMG and the NSCG for the following types of melanoma:

- Hereditary melanoma for "any individual with a personal history of or first-degree relative with (i) three or more melanomas in the same person or (ii) three or more cases of melanoma and/or pancreatic cancer (Hampel et al., 2015)."
- Melanoma-astrocytoma syndrome for "any individual with a personal history of or first-degree relative with (i) melanoma and astrocytoma in the same person or (ii) one case of melanoma and one case of astrocytoma in two first-degree relatives (Hampel et al., 2015)."
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Federal Applicable Regulations

A search on the FDA database on 10/30/2020 with the term "cutaneous melanoma" identified two results; however, both of these tests are non-invasive tools which utilize electrical impedance spectroscopy and light from visible to near-infrared wavelengths to evaluate skin lesions. Additional tests may be considered laboratory developed tests (LDTs); developed, validated and performed by individual laboratories. LDTs are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA'88). As an LDT, the U. S. Food and Drug Administration has not approved or cleared this test; however, FDA clearance or approval is not currently required for clinical use.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: 81167, 81216, 81217, 81345, 81404, 81479

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

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Policy Implementation/Update Information

For policy titled: Genetic Expression Profiling and Genetic Testing for Familial Cutaneous Malignant Melanoma

1/1/2019 BCBSNC will not provide coverage for genetic expression profiling and genetic testing for familial cutaneous malignant melanoma because it is considered investigational. BCBSNC does not provide coverage for investigational services or procedures. Medical Director review 1/1/2019. Policy noticed 1/1/2019 for effective date 4/1/2019. (jd)

4/1/2019 Description section, policy guidelines, and references updated. Medical Director review. (jd)

10/29/19 Wording in the Policy, When Covered, and/or Not Covered section(s) changed from Medical Necessity to Reimbursement language, where needed. No changes to Policy Statements. (hb)

For policy titled: Genetic Testing for Familial Cutaneous Malignant Melanoma

2/11/20 Annual review by Avalon 4th Quarter 2019 CAB. Title change. Removed the following from the When Not Covered section: "Genetic expression profiling testing for cutaneous melanoma is considered investigational." Medical Director review 12/2019. (jd)

4/14/20 Specialty Matched Consultant Advisory Panel review 3/2020. Medical Director review 3/2020. (jd)

2/9/21 Annual review by Avalon 4th Quarter 2020 CAB. Added "Related Policies" to Description section. Revised investigational statement as follows: "Genetic testing for inherited forms of melanoma is considered investigational." Policy guidelines and references updated. No change to policy intent. The following codes were added to the Billing/Coding section: 81167, 81216, 81217, 81345; the following codes were removed: 81445 and 81455. Medical Director review 1/2021. (jd)

3/31/21 Specialty Matched Consultant Advisory Panel review 3/2021. Medical Director review 3/2021. (jd)