June 11, 2018

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Omaha, NE 68164

Re: Draft Local Coverage Determination: MolDX: Comprehensive Genomic Profiling to Guide Treatment in Patients with Metastatic Melanoma (DL37220)

Dear Dr. Awodele,

Thank you for this opportunity to respond to your draft local coverage determination regarding MolDX: Comprehensive Genomic Profiling (CGP) to Guide Treatment in Patients with Metastatic Melanoma DL37220. The Association for Molecular Pathology (AMP) is an international medical professional association representing approximately 2,300 physicians, doctoral scientists, and medical technologists who perform or are involved with laboratory testing based on knowledge derived from molecular biology, genetics and genomics. Membership includes professionals from the government, academic and commercial clinical laboratories, community hospitals, and the in vitro diagnostics industry.

As the world's largest organization of board-certified pathologists and leading provider of laboratory accreditation and proficiency testing programs, the College of American Pathologists (CAP) serves patients, pathologists, and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide.

Members of both AMP and the CAP are experts in molecular pathology and the implementation of this coverage policy will directly impact their practices. We are submitting joint comments because at this time both of our organizations share the same concerns regarding this draft LCD.

Proposed Coverage for Comprehensive Genomic Profiling

AMP and the CAP applaud WPS for proposing coverage for comprehensive genomic profiling (CGP), which typically uses next generation sequencing (NGS)-based strategies. The National Comprehensive Cancer Network (NCCN) guidelines are updated on an annual basis and are based on the most current medical evidence (NCCN Melanoma Guideline 2018). Similarly the European Society for Medical Oncology (ESMO) publishes evidence-based guidelines for melanoma on a regular basis (Dumer et al 2015). Both NCCN and ESMO guidelines for melanoma require multi-gene testing for patients with advanced disease or clinical recurrence. Laboratories can meet these guidelines using a panel of single tests or by NGS methods. Despite the consensus on clinical benefits of NGS-based CGP, we believe that this draft LCD proposal is unreasonably restrictive, and we would like to work with you to improve coverage policy for patients with melanoma – to avoid inappropriate denials for CGP coverage, which will occur due to restrictions in this overly stringent draft policy.

Our predominant concern with this draft LCD is that the policy, as drafted, will severely restrict patient access to testing, given the extremely specific (and unjustified) testing requirements. If the draft LCD remains unchanged, for all practical purposes it is applicable to only a very limited number of laboratories in the entire country. Our comments outline changes supported by the medical literature that would broaden this restrictive testing criteria so that more high-quality, stringently compliant laboratories would also be able offer this clinically-proven testing to their patients.

We have found no evidence in the scientific literature that many of the requirements outlined in this policy improve downstream clinical decisions. Limiting coverage to the very small number of labs currently meeting these criteria will significantly restrict access to testing without a justifiable improvement in clinical decision making – and could, unintentionally, even worsen outcomes by delaying or preventing the genomic tests that often inform optimal therapies. In addition to the limitations in patient access to testing that will be caused by this overly stringent policy, the concomitant lack of competition in the testing space could also lead to a downturn in quality and an increase in testing costs. Furthermore, clinical research trials into new targeted cancer therapies will become more expensive and available in fewer locations due to the restricted access to testing and lack of competition.

We also remain very concerned, as detailed in previous LCD responses, about whether WPS has the statutory authority to regulate LDTs (and their analytical and clinical validity), which typically fall under the purview of CLIA.

CGP Test Description

In the policy, CGP analysis is defined as a single test using tumor tissue only (i.e., not matched tumor and normal) that can detect all of the following classes of alternations and genomic information in a single test: base pair substitutions; insertions and deletions; copy number variations; rearrangements; microsatellite instability (MSI); and tumor mutational burden (TMB). WPS states that other non-NGS testing platforms may be considered if they can similarly detect all classes of alterations and genomic information with comparable test performance as CGP. Tumor mutation burden should be considered a subclass of base pair substitutions, rather than a separate class of genomic alternation since TMB is defined by the literature as the number of exonic single nucleotide substitutions (Rizvi et al 2015). Similarly, microsatellite instability is defined as the expansion of or contraction of mononucleotide, dinucleotide, trinucleotide repeats, etc. and should be considered a subclass of the "indel" genomic alteration (i.e. insertion or deletion of nucleotides) (Salipante et al 2014).

Several groups have published CGP validation studies showing the utility of paired normal tissue for improving the analysis of DNA sequencing (Luthra et al 2017, Ross et al 2017). Consequently, CGP analysis should also include covered assays that used matched tumor and normal since this approach offers high quality CGP results. Extra reimbursement for those labs that choose to sequence matched normal tissue (as a quality control exercise) is not justified.

We believe that requiring the detection of all the listed classes of genomic alterations within a single procedure is not necessary, is overly burdensome to laboratories that use alternative technical approaches to provide the comparable findings, and does little to guide treatment and increase benefit to the patient. Medical necessity must be paramount in any coverage determination and the medical necessity for detecting all the listed classes of genomic alterations has not been rigorously established. Moreover, there is no medical literature that suggests multiple genomic aberrations need to be detected by a "single test", as mandated on page 5 of the draft LCD. For

example, there are technologies such as SNP-based microarray that can detect genome wide copy number alterations in a sensitive and cost-efficient fashion. Targeted translocations and copy number alterations can also be detected by FISH and PCR-based methods. **We, therefore, recommend altering this policy to:**

1. **NOT require the detection of all the listed classes of genomic alterations;**
2. **NOT require the detection of all alterations in a single assay, and**
3. **Allow coverage consideration for laboratories that incorporate diverse and complimentary multi-test (not "single test") technologies to detect the listed classes of genomic alterations.**

Recommendations Regarding the Proposed Coverage Requirements

AMP and the CAP are supportive of WPS' proposal to cover CGP analysis using multiplex or NGS technology, recognizing that this testing is reasonable and necessary to guide targeted therapy (e.g. BRAF/MEK inhibitor) and possibly for immuno-oncology therapy in patients with melanoma (Van Allen E.M. et al. 2015). We disagree that all eight of the criteria listed in the draft LCD must be met and combined into a "single test" to qualify as medically necessary. As detailed above, these overly stringent criteria will limit CGP testing for melanoma, for all practical purposes, to only a very few laboratories that have chosen, for commercial purposes, to market their assay as a "single test". We recommend that these criteria be revised to reflect the content in the NCCN guidelines.

The policy states the following:

CGP analysis using multiplex or next generation sequencing technology is reasonable and necessary to guide targeted and/or immune-oncology patients with metastatic melanoma when ALL of the following criteria are met.

AMP and the CAP recommend that the words "ALL of" be struck from this sentence.

We have further recommendations for revisions to the eight specific testing criteria outlined in the draft LCD. In particular, we recommend:

Criterion One

"Patient has been newly diagnosed with stage 4 metastatic melanoma."

Both, NCCN and ESMO guidelines for melanoma require multi-gene testing, typically performed with next generation sequencing (NGS), in patients with advanced disease (unresectable stage III or stage IV) or at clinical recurrence regardless of presentation stage (Dummer et al 2015, NCCN Melanoma Guideline 2018, see NCCN ME- 8,9,10). ESMO guidelines also highly recommend mutation analysis in high-risk resected melanoma (stage IIc, stage IIIb–IIIc) at presentation.

AMP and the CAP recommend changing criterion one to reflect current NCCN and ESMO guidelines.

Criterion Two

"Patient has not been tested for genomic alterations via CGP methods or PCR techniques."

Both NCCN and ESMO guidelines for melanoma require multi-gene testing for the "treatable mutations" BRAF and KIT in the appropriate clinical context. ESMO guidelines state that "if the tumor is BRAF-wild type, testing for NRAS mutations & c-kit mutation should be considered. " Consequently, routine clinical work up for

melanoma patients will usually be limited to these genes (BRAF, KIT, NRAS) at the request of the treating oncologist. This sequential targeted approach is less expensive and can offer more rapid results for the patient. Oncologists often request comprehensive genomic profiling only in instances when patients are unlikely to respond to, or fail, standard therapy in order to guide clinical decision making for enrollment in a clinical trial.

This criterion will place an undue financial burden on hospital labs that provide a targeted panel for "treatable mutations" prior to an oncologist's request for comprehensive genomic profiling (CGP). In this scenario the laboratory performing the "second" CGP test would not be paid for the cost of performing the test, given the prior targeted test had occurred. For hospital labs that offer a "targeted" panel but do not perform CGP, the current Medicare rules require the outside CGP laboratory to bill a hospital for pathology technical component services for Medicare inpatients. Based on this criterion the hospital will be unable to bill Medicare for the substantial additional cost of outside CGP laboratory services. Compliance with NCCN/ESMO guidelines will lead to a tiered testing approach for patients who are unlikely to respond to, or fail, standard therapies. Further, patients with recurrence may require testing of more than one specimen (i.e. at presentation and at clinical recurrence).

AMP and the CAP recommend changing criterion two to reflect NCCN/ESMO guidelines and the reality of clinical practice in oncology.

Criterion Four

"The CGP is a hybrid-capture based NGS genomic testing platform that can detect all four types of DNA alterations seen in cancer – base pair substitutions, small indels, copy number alterations and rearrangements – in hundreds of cancer-related genes with high sensitivity and specificity that has been validated in a peer-reviewed journal(s)"

a) This is a very restrictive approach, dictating laboratory specific methodology, despite evidence that this approach is not the only effective one. Many NGS-based strategies employ amplicon based library preparation, which are equally effective as hybrid-capture to identify these genomic aberrations (Luthra R et al. 2017). Specifically, a large, multi-site trial sponsored by the National Cancer Institute, Molecular Analysis for Therapy Choice (NCI-MATCH), has deployed genomic testing that is amplicon-based, not hybrid-capture based. This testing strategy was thoroughly investigated prior to deployment and has been successfully utilized to detect the DNA alterations described above (Chih-Jian Lih et al. 2017). For example, in the cohort tested, the 143 gene Oncomine Comprehensive Assay -Proton assay detected 145 of 148 SNVs (97.9% sensitivity), 48 of 49 indels (97.9% sensitivity), and all 40 CNVs (100% sensitivity) indicating an overall average sensitivity of 98.6%. The intent of the study is to screen thousands of patients with this assay, and the assay's manufacturer, Thermo Fisher Scientific, has submitted a premarket Approval Application to the FDA in November of 2016. Thus, the provision in this LCD indicating a specific required hybrid capture methodology does not take into account the current state of the art in laboratory science and could lead to significantly decreased patient access to testing. The requirements for an assay that is "*hybrid capture-based*" should thus be deleted.
b) The requirements for an assay that detects aberrations in "*hundreds of cancer related genes*" should be deleted. The number of clinically "actionable" genomic gene targets is a matter of considerable scientific debate, and many laboratories offer clinically validated NGS-based testing that targets less than "hundreds" of genes, yet is considered comprehensive for clinically "actionable" therapies. We recommend that the required genes be limited to those included in the current NCCN and ESMO guidelines. e.g. BRAF, KIT, and NRAS are considered necessary for therapeutic decision making.

c) The requirement for an assay that has been "validated in a peer-reviewed journal" falls outside requirements of any current regulatory framework and should be deleted. We are unaware of any precedent in the history of CMS laboratory medicine coverage policy that any assay be "validated in a peer-reviewed journal". Many extensively validated CGP assays are developed in non-academic reference laboratories whose commercial mission often does not prioritize publication in a peer-reviewed medical journal. Even FDA does not mandate publication of assay validation details in a peer-reviewed journal. Additionally, despite completing rigorous validations as dictated by CLIA, many laboratories may decide not to pursue an academic publication, if similar or identical assay validations have already been published in a peer-reviewed journal.

Criterion Five

"The laboratory providing CGP testing services must meet the minimum requirements of being CLIA-certified, CAP-accredited and approved by the New York State Department of Health…"

2018 NCCN guidelines for melanoma state BRAF mutational status should be tested using an FDA-approved test or by a facility approved by Clinical Laboratory Improvement Amendments (CLIA). The New York State Department of Health's (NYSDOH) requires premarket review by Clinical Laboratory Evaluation Program (CLEP) if the test is performed in New York State or the sample is from New York State. The WPS jurisdictions are J5 and J8. Laboratories within the WPS jurisdictions do not test patient samples from New York state unless they have a large outreach business serving patients in New York. In the State of New York, CLEP compliance supersedes other forms of accreditation to avoid duplicative requirements, but this does not apply to labs in the WPS jurisdictions that would require multiple rounds of certification. The "New York State" requirement would place an unnecessary financial and regulatory burden on laboratories that serve only a local patient population. As such, this criterion will act as an impediment to laboratory adoption of CGP assays and is likely to reduce local cancer patient's access to this testing.

We recommend that WPS strike the requirement for New York State Department of Health approval. Since the MolDx program's policies are now applied in approximately half the country, AMP and the CAP believe it would not only be appropriate, but legally required, that testing requirements comply with the Department of Health and Human Services' national regulations, rather the requirements of any single state's health department. Specifically, we recommend the requirement be altered to state that the lab be "CLIA-certified or equivalent, as required." The draft policy requirement, as written, implies that all laboratories – whether or not they provide services to patients in the state of New York – must be certified by the New York State Department of Health.

Criterion Six

"The CGP result will report out all known BRAF mutations, KRAS mutations, KIT mutations, TMB, MSI, CDKN2A mutations, and other appropriate familial genetic abnormalities causing melanoma; and potentially provide direction to an expert in hereditary cancer risk assessment or other specialist (e.g. gastroenterology) when CDKN2A, CDK4, BRCA1 or BRCA2 alternation is identified to determine if a hereditary cancer syndrome exists"

NCCN guidelines require BRAF and KIT mutation testing for therapeutic decision making. FDA-approved targeted therapies are available for melanoma patients with BRAF mutations (vemurafenib (Zelboraf®), dabrafenib (Tafinlar®)) and for melanoma patients with KIT mutations (Imatinib mesylate (Gleevec®)).

NRAS not KRAS mutations are common in melanoma, and like KRAS mutations, confer resistance to BRAF V600E inhibitors (vemurafenib (Zelboraf®) dabrafenib (Tafinlar®). Melanoma patients with NRAS mutations may benefit from MEK kinase-inhibitor therapy trametinib (Mekinist®) (Ascierto et al 2013, Dummer et al. 2015).

NCCN guidelines require multi-gene testing for "prognostic mutations " (ie. EIF1AX, SF3B1, BAP1 and PRAME) or copy number alterations (ie. Chromosome 6p or 8q gains, 3 monosomy/disomy) in patients with uveal melanoma. This testing is medically necessary to schedule systemic imaging and blood testing based on risk stratification determined by this genetic testing (NCCN Uveal Melanoma 2018 Ver1 UM-4).

Current NCCN guidelines also recommend molecular testing for histologically equivocal lesions. For instance, a GNAQ or GNA11 mutation can be used to differentiate metastatic uveal melanoma from metastatic cutaneous melanoma (Cornejo et al 2013). The presence of an HRAS mutation can distinguish a benign "atypical" spitz tumor from a malignant spitz melanoma (vanEngen-vanGrunsve et al 2010).

TMB and MSI: TMB and MSI testing, which is used to identify patients that may benefit from immunotherapy, is medically unnecessary for patients with melanoma since the diagnosis already confers FDA eligibility for immunotherapy (ipilimumab (Yervoy®), pembrolizumab (Keytruda®), nivolumab (Opdivo®) and avelumab (Bavencio®)).

TMB: Elevated nonsynonymous mutation load has been associated with response to ipilimumab, yet melanoma patients with long-term survival had low mutational load (Van Allen E.M. et al. 2015). Consequently, this approach may enrich for patients who benefit from immunotherapy, but should not be used to exclude patients from therapy. Data supporting this approach for therapeutic selection is immature in the literature, and mandating its deployment is not consistent with current guidelines.

MSI: Microsatellite instability is most commonly associated with mutations in mismatch repair proteins (e.g. MLH1/PMS2, MSH2/MSH6) and is usually observed in Lynch syndrome tumors such as colorectal carcinoma, endometrial carcinoma, sebaceous adenoma/carcinoma of the skin, small bowel, urinary tract). Currently NCCN and ESMO guidelines do not mention MSI testing for melanoma patients. The literature provides limited evidence for mismatch repair defects in rare instances of melanoma (Ponti et al. 2008, Karamurzin et al. 2011, Lobo et al. 2017).

Familial Genetic Abnormalities: NCCN guidelines recognize genetic predisposition associated with "presence of melanoma susceptibility polymorphisms (including CDKN2A, CDK4, MC1R, and other as yet undetermined germline mutations). NCCN guidelines state "consider testing in the presence of 3 or more invasive melanomas or a mix of invasive melanoma and pancreatic cancer diagnoses in an individual or family." Currently NCCN and ESMO guidelines do not mention BRCA1 or BRCA2. The literature shows that BRCA carriers may carry an increased risk for melanoma but represent a small percentage of melanoma patients (<2%) (Ginsburg OM et al 2010). Since this draft LCD defines CGP as "a single test using tumor tissue only (i.e., not matched tumor and normal)" this approach may detect a significant number of mutations in genes listed above that are somatic rather than hereditary germline in nature. This approach encompasses the extra expense of additional genetic testing of a non-tumor sample and this testing is not currently covered by Medicare in any jurisdiction.

AMP and the CAP recommend changing criterion six to reflect the genes/mutations referred to in current NCCN and ESMO guidelines or genes recognized in the literature as having clinical utility. We, therefore, recommend that criterion six be revised as follows "The panel includes established biomarkers such as BRAF mutations,

NRAS mutations, KIT mutations and may also include emerging biomarkers such as TMB and MSI. CDKN2A mutations, and other appropriate familial genetic abnormalities causing melanoma should be reported in the appropriate clinical context; and potentially provide direction to an expert in hereditary cancer risk assessment or other specialist (e.g. oncologist) when an alteration may suggest a hereditary cancer syndrome. Such alterations may include but are not limited to the following genes: *CDKN2A, CDK4, MC1R."*

Criterion Eight

WPS requires the following: *Testing is performed with an assay that has been reviewed via the MolDX Technical Assessment process and is listed as a "Covered Test" on the MolDx website.*

AMP and the CAP continue to disagree that the MolDX program technical assessment requirement is necessary to review the analytic validity of each LDT or modified IVD. In order to be reimbursed by Medicare, the laboratory must be CLIA certified. CMS has already certified the laboratory (and all the tests it performs) under the CLIA program, which sets a standard for quality control for all tests performed. Analytical validity is thus already substantively addressed by CLIA regulations, which require laboratories to demonstrate analytical validity and regular proficiency testing. Assuring clinical validity is not directly evaluated by CLIA. In particular, CLIA regulations under 42 CFR § 493.1445(e)(3)(i) require the laboratory director and technical supervisor to ensure that selected test methodologies are capable of providing the quality of results required for patient care. Implicit in this regulation is the responsibility of the laboratory director to use medically relevant test methodologies that have an effective clinical purpose—otherwise those methodologies could not be said to be "required for patient care" (U.S. System of Oversight of Genetic Testing). Thus, the effective clinical purpose or clinical validity is typically documented by the laboratory in review of medical literature. If a lab is not CLIA certified, the test cannot be paid for by Medicare.

CPT Coding

We note that the draft LCD mandates the use of molecular, NOS CPT coding (81479) for submission of claims. This approach is in stark contradiction to previous requirements from MolDx to exclusively utilize the most appropriate existing CPT code. In this case, existing genomic sequencing codes (81445, 81455) appropriately describe the scope of services proposed in this LCD. Specifically, the existing codes note the inclusion of 'interrogation for sequence variants and copy number variants or rearrangements, if performed'. All classes of alterations described in this LCD are included in this CPT descriptor. Tumor mutation burden and MSI, when performed as part of a next generation sequencing based assay, are bioinformatic derivatives of single nucleotide alterations and insertion/deletion alterations. For instance, MSI testing commonly relies on the analysis detection of insertion/deletions in 5 genes (KIT [BAT-25], MSH2 [BAT-26], SLC7A8 [NR-21], ZNF-2 [NR-24], MAP4K3 [MONO-27] either by fragment analysis (Bacher JW et al. 2004) or by NGS sequencing (Hempelmann JA et al. 2015). Thus, it would be inappropriate for WPS to require a non- specific "not otherwise specified" CPT code, given the existence of a CPT code which appropriately describes the scope of services. A precedent also exists in previously finalized LCDs from National Government Services that uses the CPT codes 81445 and 81450 for Genomic Sequence Analysis Panels in the Treatment of Non-Small Cell Lung Cancer (L36376) or Acute Myelogenous Leukemia (L36926). **Therefore we recommend the use of CPT codes 81445 and 81455 (rather than 81479) to fulfill criteria for CGP testing, analogous to the LCD from WPS on Non-Small Cell Lung Cancer.**

If an individual laboratory's assay is sufficiently unique such that existing CPT codes do not appropriately apply to the assay, the laboratory should endeavor to have its assay recognized through appropriate channels, which would require obtaining a Proprietary Laboratory Analyses (PLA) code through the American Medical Association's CPT Editorial Panel process, rather than inappropriate utilization of 81479 as suggested in this LCD.

The criteria for CGP can also be fulfilled with additional CPT codes that WPS did not include in its draft policy proposal. For example, consideration may also be given to other CPT codes that would include PCR-based testing (eg. BRAF 81210, KIT 81272, KRAS1 81275, KRAS2 81276, NRAS 81311, ORAME 81401, GNAQ 81403, HRAS 81403), FISH (eg 88366), and/or cytogenomic microarray.

ICD-10 Coding

The proposed policy lists a limited set of ICD-10 codes as supporting medical necessity, primarily associated with cutaneous melanomas. We are concerned that codes covering additional primary melanoma lesions (eg uveal melanomas, mucosal melanomas) and metastatic melanoma should also be included in order to more accurately account for all types of tumors that may be encountered. In addition The ICD-10 codes in the current policy do not accommodate patients who present with histologically equivocal lesions (eg. Atypical nevi versus malignant melanoma versus undifferentiated sarcoma). For example, a patient may present with a clinical diagnosis of basal cell or squamous cell carcinoma or dysplastic neve but the histological diagnosis is equivocal. These patients require molecular testing to demonstrate melanoma. Consequently, we request addition of ICD-10 codes associated with the appropriate clinical criteria raising the suspicion of melanoma and triggering the oncologist's request for this testing.

We request that additional ICD-10 codes added to this policy include, but not be limited to the following list:

C06.9	Malignant melanoma of mouth
C15.9	Melanoma of esophagus
C20	Malignant melanoma of rectum
C21.0	Melanoma of anus
C21.1	Melanoma of anal canal
C23	Melanoma of gallbladder
C25.9	Melanoma-pancreatic cancer syndrome
C30	Melanoma of nasal cavity
C31.3	Malignant melanoma of sphenoidal sinus
C31.9	Malignant melanoma of accessory sinus
C43	Malignant melanoma of skin
C43.1	Malignant melanoma of eyelid, including canthus
C43.2	Malignant melanoma of ear and external auricular canal
C43.3	Malignant melanoma of other and unspecified parts of face
C43.4	Malignant melanoma of scalp and neck
C43.5	Malignant melanoma of trunk
C43.6	Malignant melanoma of upper limb, including shoulder
C43.7	Malignant melanoma of lower limb, including hip
C44	Other and unspecified malignant neoplasm of skin
C44.0	Other and unspecified malignant neoplasm of skin of lip
C44.00	Unspecified malignant neoplasm of skin of lip
C44.01	Basal cell carcinoma of skin of lip
C44.02	Squamous cell carcinoma of skin of lip
C44.09	Other specified malignant neoplasm of skin of lip
C44.1	Other and unspecified malignant neoplasm of skin of eyelid, including canthus
C44.10	Unspecified malignant neoplasm of skin of eyelid, including canthus
C44.101	Unspecified malignant neoplasm of skin of unspecified eyelid, including canthus
C44.102	Unspecified malignant neoplasm of skin of right eyelid, including canthus

C44.109	Unspecified malignant neoplasm of skin of left eyelid, including canthus
C44.11	Basal cell carcinoma of skin of eyelid, including canthus
C44.111	Basal cell carcinoma of skin of unspecified eyelid, including canthus
C44.112	Basal cell carcinoma of skin of right eyelid, including canthus
C44.119	Basal cell carcinoma of skin of left eyelid, including canthus
C44.12	Squamous cell carcinoma of skin of eyelid, including canthus
C44.121	Squamous cell carcinoma of skin of unspecified eyelid, including canthus
C44.122	Squamous cell carcinoma of skin of right eyelid, including canthus
C44.129	Squamous cell carcinoma of skin of left eyelid, including canthus
C44.19	Other specified malignant neoplasm of skin of eyelid, including canthus
C44.191	Other specified malignant neoplasm of skin of unspecified eyelid, including canthus
C44.192	Other specified malignant neoplasm of skin of right eyelid, including canthus
C44.199	Other specified malignant neoplasm of skin of left eyelid, including canthus
C44.2	Other and unspecified malignant neoplasm of skin of ear and external auricular canal
C44.20	Unspecified malignant neoplasm of skin of ear and external auricular canal
C44.201	Unspecified malignant neoplasm of skin of unspecified ear and external auricular canal
C44.202	Unspecified malignant neoplasm of skin of right ear and external auricular canal
C44.209	Unspecified malignant neoplasm of skin of left ear and external auricular canal
C44.21	Basal cell carcinoma of skin of ear and external auricular canal
C44.211	Basal cell carcinoma of skin of unspecified ear and external auricular canal
C44.212	Basal cell carcinoma of skin of right ear and external auricular canal
C44.219	Basal cell carcinoma of skin of left ear and external auricular canal
C44.22	Squamous cell carcinoma of skin of ear and external auricular canal
C44.221	Squamous cell carcinoma of skin of unspecified ear and external auricular canal
C44.222	Squamous cell carcinoma of skin of right ear and external auricular canal
C44.229	Squamous cell carcinoma of skin of left ear and external auricular canal
C44.29	Other specified malignant neoplasm of skin of ear and external auricular canal
C44.291	Other specified malignant neoplasm of skin of unspecified ear and external auricular canal
C44.292	Other specified malignant neoplasm of skin of right ear and external auricular canal
C44.299	Other specified malignant neoplasm of skin of left ear and external auricular canal
C44.3	Other and unspecified malignant neoplasm of skin of other and unspecified parts of face
C44.30	Unspecified malignant neoplasm of skin of other and unspecified parts of face
C44.300	Unspecified malignant neoplasm of skin of unspecified part of face
C44.301	Unspecified malignant neoplasm of skin of nose
C44.309	Unspecified malignant neoplasm of skin of other parts of face
C44.31	Basal cell carcinoma of skin of other and unspecified parts of face
C44.310	Basal cell carcinoma of skin of unspecified parts of face
C44.311	Basal cell carcinoma of skin of nose
C44.319	Basal cell carcinoma of skin of other parts of face
C44.32	Squamous cell carcinoma of skin of other and unspecified parts of face
C44.320	Squamous cell carcinoma of skin of unspecified parts of face
C44.321	Squamous cell carcinoma of skin of nose
C44.329	Squamous cell carcinoma of skin of other parts of face
C44.39	Other specified malignant neoplasm of skin of other and unspecified parts of face
C44.390	Other specified malignant neoplasm of skin of unspecified parts of face
C44.391	Other specified malignant neoplasm of skin of nose
C44.399	Other specified malignant neoplasm of skin of other parts of face

C44.4 Other and unspecified malignant neoplasm of skin of scalp and neck
C44.40 Unspecified malignant neoplasm of skin of scalp and neck
C44.41 Basal cell carcinoma of skin of scalp and neck
C44.42 Squamous cell carcinoma of skin of scalp and neck
C44.49 Other specified malignant neoplasm of skin of scalp and neck
C44.5 Other and unspecified malignant neoplasm of skin of trunk
C44.50 Unspecified malignant neoplasm of skin of trunk
C44.50 Unspecified malignant neoplasm of anal skin
C44.50 Unspecified malignant neoplasm of skin of breast
C44.50 Unspecified malignant neoplasm of skin of other part of trunk
C44.51 Basal cell carcinoma of skin of trunk
C44.51 Basal cell carcinoma of anal skin
C44.51 Basal cell carcinoma of skin of breast
C44.51 Basal cell carcinoma of skin of other part of trunk
C44.52 Squamous cell carcinoma of skin of trunk
C44.52 Squamous cell carcinoma of anal skin
C44.52 Squamous cell carcinoma of skin of breast
C44.52 Squamous cell carcinoma of skin of other part of trunk
C44.59 Other specified malignant neoplasm of skin of trunk
C44.59 Other specified malignant neoplasm of anal skin
C44.59 Other specified malignant neoplasm of skin of breast
C44.59 Other specified malignant neoplasm of skin of other part of trunk
C44.6 Other and unspecified malignant neoplasm of skin of upper limb, including shoulder
C44.60 Unspecified malignant neoplasm of skin of upper limb, including shoulder
C44.60 Unspecified malignant neoplasm of skin of unspecified upper limb, including shoulder
C44.60 Unspecified malignant neoplasm of skin of right upper limb, including shoulder
C44.60 Unspecified malignant neoplasm of skin of left upper limb, including shoulder
C44.61 Basal cell carcinoma of skin of upper limb, including shoulder
C44.61 Basal cell carcinoma of skin of unspecified upper limb, including shoulder
C44.61 Basal cell carcinoma of skin of right upper limb, including shoulder
C44.61 Basal cell carcinoma of skin of left upper limb, including shoulder
C44.62 Squamous cell carcinoma of skin of upper limb, including shoulder
C44.62 Squamous cell carcinoma of skin of unspecified upper limb, including shoulder
C44.62 Squamous cell carcinoma of skin of right upper limb, including shoulder
C44.62 Squamous cell carcinoma of skin of left upper limb, including shoulder
C44.69 Other specified malignant neoplasm of skin of upper limb, including shoulder
C44.69 Other specified malignant neoplasm of skin of unspecified upper limb, including shoulder
C44.69 Other specified malignant neoplasm of skin of right upper limb, including shoulder
C44.69 Other specified malignant neoplasm of skin of left upper limb, including shoulder
C44.7 Other and unspecified malignant neoplasm of skin of lower limb, including hip
C44.70 Unspecified malignant neoplasm of skin of lower limb, including hip
C44.70 Unspecified malignant neoplasm of skin of unspecified lower limb, including hip
C44.70 Unspecified malignant neoplasm of skin of right lower limb, including hip
C44.70 Unspecified malignant neoplasm of skin of left lower limb, including hip
C44.71 Basal cell carcinoma of skin of lower limb, including hip
C44.71 Basal cell carcinoma of skin of unspecified lower limb, including hip
C44.71 Basal cell carcinoma of skin of right lower limb, including hip

C44.719	Basal cell carcinoma of skin of left lower limb, including hip
C44.72	Squamous cell carcinoma of skin of lower limb, including hip
C44.721	Squamous cell carcinoma of skin of unspecified lower limb, including hip
C44.722	Squamous cell carcinoma of skin of right lower limb, including hip
C44.729	Squamous cell carcinoma of skin of left lower limb, including hip
C44.79	Other specified malignant neoplasm of skin of lower limb, including hip
C44.791	Other specified malignant neoplasm of skin of unspecified lower limb, including hip
C44.792	Other specified malignant neoplasm of skin of right lower limb, including hip
C44.799	Other specified malignant neoplasm of skin of left lower limb, including hip
C44.8	Other and unspecified malignant neoplasm of overlapping sites of skin
C44.80	Unspecified malignant neoplasm of overlapping sites of skin
C44.81	Basal cell carcinoma of overlapping sites of skin
C44.82	Squamous cell carcinoma of overlapping sites of skin
C44.89	Other specified malignant neoplasm of overlapping sites of skin
C44.9	Other and unspecified malignant neoplasm of skin, unspecified
C44.90	Unspecified malignant neoplasm of skin, unspecified
C44.91	Basal cell carcinoma of skin, unspecified
C44.92	Squamous cell carcinoma of skin, unspecified
C44.99	Other specified malignant neoplasm of skin, unspecified
C49.9	Melanoma, malignant, of soft parts (CMS/HCC)
C51.0	Mucoscal Melanoma of labia majora (CMS/HCC)
C51.9	Melanoma of vulva (CMS/HCC)
C52	Melanoma of vagina (CMS/HCC)
C60.0	Melanoma of foreskin (CMS/HCC)
C60.9	Melanoma of skin of penis (CMS/HCC)
C63.2	Malignant melanoma of skin of scrotum (CMS/HCC)
C69	Melanoma of conjunctiva (CMS/HCC)
C69.00	Melanoma of conjunctiva, unspecific laterality (CMS/HCC)
C69.01	Melanoma of conjunctiva, right (CMS/HCC)
C69.02	Melanoma of conjunctiva, left (CMS/HCC)
C69.10	Malignant melanoma of cornea (CMS/HCC)
C69.11	Malignant melanoma of cornea, right
C69.12	Malignant melanoma of cornea, left
C69.30	Melanoma, choroid
C69.31	Melanoma, choroid right eye
C69.32	Melanoma, choroid left eye
C69.40	Melanoma of uvea (CMS/HCC)
C69.41	Melanoma of uvea, right (CMS/HCC)
C69.42	Melanoma of uvea, left (CMS/HCC)
C69.60	Melanoma of orbit (CMS/HCC)
C69.90	Malignant neoplasm of unspecified site of unspecified eye
C69.91	Malignant neoplasm of unspecified site of right eye
C69.92	Malignant neoplasm of unspecified site of left eye
C70.0	Leptomeningeal melanoma of brain
C77.1	Secondary and unspecified malignant neoplasm of intrathoracic lymph nodes
C77.2	Secondary and unspecified malignant neoplasm of intra-abdominal lymph nodes
C77.3	Secondary and unspecified malignant neoplasm of axilla and upper limb lymph nodes
C77.4	Secondary and unspecified malignant neoplasm of inguinal and lower limb lymph nodes

C77.5	Secondary and unspecified malignant neoplasm of intrapelvic lymph nodes
C77.8	Secondary and unspecified malignant neoplasm of lymph nodes of multiple regions
C77.9	Secondary and unspecified malignant neoplasm of lymph node, unspecified (melanoma
C78	Secondary malignant neoplasm of respiratory and digestive organs
C78.0	Secondary malignant neoplasm of lung
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.1	Secondary malignant neoplasm of mediastinum
C78.2	Secondary malignant neoplasm of pleura
C78.3	Secondary malignant neoplasm of other and unspecified respiratory organs
C78.30	Secondary malignant neoplasm of unspecified respiratory organ
C78.39	Secondary malignant neoplasm of other respiratory organs
C78.4	Secondary malignant neoplasm of small intestine
C78.5	Secondary malignant neoplasm of large intestine and rectum
C78.6	Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
C78.8	Secondary malignant neoplasm of other and unspecified digestive organs
C78.80	Secondary malignant neoplasm of unspecified digestive organ
C78.89	Secondary malignant neoplasm of other digestive organs (
C79	Secondary malignant neoplasm of other and unspecified sites
C79.0	Secondary malignant neoplasm of kidney and renal pelvis
C79.00	Secondary malignant neoplasm of unspecified kidney and renal pelvis
C79.01	Secondary malignant neoplasm of right kidney and renal pelvis
C79.02	Secondary malignant neoplasm of left kidney and renal pelvis
C79.3	Secondary malignant neoplasm of brain and cerebral meninges
C79.31	Secondary malignant neoplasm of brain (melanoma metastatic to brain)
C79.32	Secondary malignant neoplasm of cerebral meninges
C79.5	Secondary malignant neoplasm of bone and bone marrow
C79.51	Secondary malignant neoplasm of bone (melanoma metastatic to bone)
C79.52	Secondary malignant neoplasm of bone marrow
C80.0	Leptomeningeal melanoma determined by biopsy of brain (CMS/HCC)
D03	Melanoma in situ
D03.0	Melanoma in situ of lip
D03.1	Melanoma in situ of eyelid, including canthus
D03.10	Melanoma in situ of unspecified eyelid, including canthus
D03.11	Melanoma in situ of right eyelid, including canthus
D03.12	Melanoma in situ of left eyelid, including canthus
D03.2	Melanoma in situ of ear and external auricular canal
D03.20	Melanoma in situ of unspecified ear and external auricular canal
D03.21	Melanoma in situ of right ear and external auricular canal
D03.22	Melanoma in situ of left ear and external auricular canal
D03.3	Melanoma in situ of other and unspecified parts of face
D03.30	Melanoma in situ of unspecified part of face
D03.39	Melanoma in situ of other parts of face

D03.4	Melanoma in situ of scalp and neck
D03.5	Melanoma in situ of trunk
D03.51	Melanoma in situ of anal skin
D03.52	Melanoma in situ of breast (skin) (soft tissue)
D03.59	Melanoma in situ of other part of trunk
D03.6	Melanoma in situ of upper limb, including shoulder
D03.60	Melanoma in situ of unspecified upper limb, including shoulder
D03.61	Melanoma in situ of right upper limb, including shoulder
D03.62	Melanoma in situ of left upper limb, including shoulder
D03.7	Melanoma in situ of lower limb, including hip
D03.70	Melanoma in situ of unspecified lower limb, including hip
D03.71	Melanoma in situ of right lower limb, including hip
D03.72	Melanoma in situ of left lower limb, including hip
D03.8	Melanoma in situ of other sites
D03.9	Melanoma in situ, unspecified
D22	Melanocytic nevi
D22.0	Melanocytic nevi of lip
D22.1	Melanocytic nevi of eyelid, including canthus
D22.10	Melanocytic nevi of unspecified eyelid, including canthus
D22.11	Melanocytic nevi of right eyelid, including canthus
D22.12	Melanocytic nevi of left eyelid, including canthus
D22.2	Melanocytic nevi of ear and external auricular canal
D22.20	Melanocytic nevi of unspecified ear and external auricular canal
D22.21	Melanocytic nevi of right ear and external auricular canal
D22.22	Melanocytic nevi of left ear and external auricular canal
D22.3	Melanocytic nevi of other and unspecified parts of face
D22.30	Melanocytic nevi of unspecified part of face
D22.39	Melanocytic nevi of other parts of face
D22.4	Melanocytic nevi of scalp and neck
D22.5	Melanocytic nevi of trunk
D22.6	Melanocytic nevi of upper limb, including shoulder
D22.60	Melanocytic nevi of unspecified upper limb, including shoulder
D22.61	Melanocytic nevi of right upper limb, including shoulder
D22.62	Melanocytic nevi of left upper limb, including shoulder
D22.7	Melanocytic nevi of lower limb, including hip
D22.70	Melanocytic nevi of unspecified lower limb, including hip
D22.71	Melanocytic nevi of right lower limb, including hip
D22.72	Melanocytic nevi of left lower limb, including hip
D22.9	Melanocytic nevi, unspecified
D23.9	Dysplastic nevi, Multiple dysplastic nevi
Q87.89	Encounter for surveillance of abnormal nevi, Melanoma and neural system tumor syndrome
Z13.89	Epidermal nevus syndrome
Z80.8	FH: melanoma, FHx: melanoma
Z85.820	H/O melanoma excision
Z86.008	H/O melanoma in situ
Z98.890	H/O melanoma excision

We respectfully ask that you consider these comments which were prepared by expert members of AMP and the CAP who provide services to Medicare beneficiaries covered by WPS. We are happy to be of assistance in providing additional clinical information, references, contacts, or whatever is needed to assist you with this draft LCD. Please direct your correspondence to Tara Burke, AMP Director of Public Policy and Advocacy at tburke@amp.org or Nonda Wilson, the CAP's Manager, Economic and Regulatory Affairs, at nwilson@cap.org.

Sincerely,

Association for Molecular Pathology
College of American Pathologists

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