



February 27, 2023

Meredith Loveless, MD
Attn: Medical Review
26 Century Blvd., Ste ST610
Nashville, TN 37214-3685

RE: Special Histochemical Stains and Immunohistochemical Stains (DL35986)

Dear Dr. Loveless:

The National Comprehensive Cancer Network® (NCCN®) appreciates the opportunity to comment on the Cigna Government Services' (CGS) Proposed Local Coverage Determination (LCD) Special Histochemical Stains and Immunohistochemical Stains (DL35986) as it relates to NCCN's mission of improving and facilitating, quality, effective, equitable, and accessible cancer care so all patients can live better lives. NCCN is pleased to provide information and resources and will focus on the portions of the LCD with reference to NCCN Guidelines as well as the role of clinical practice guidelines and the NCCN Biomarker Compendium as a tool for establishing appropriate care.

NCCN Background

As an alliance of 32 leading academic cancer centers in the United States that treat hundreds of thousands of patients with cancer annually, NCCN® is a developer of authoritative information regarding cancer prevention, screening, diagnosis, treatment, and supportive care that is widely used by clinical professionals and payers alike. The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a comprehensive set of guidelines detailing the sequential management decisions and interventions that currently apply to 97 percent of cancers affecting patients in the United States.

NCCN Guidelines® and Library of Compendia products help ensure access to appropriate care, clinical decision-making, and assessment of quality improvement initiatives. The NCCN Drugs & Biologics Compendium (NCCN Compendium®) has been recognized by CMS and clinical professionals in the commercial payer setting since 2008 as an evidence-based reference for establishment of coverage policy and coverage decisions regarding off-label use of anticancer and cancer-related medications. NCCN was recognized by CMS in 2016 and renewed in 2021 as a qualified Provider Led Entity (PLE) for the Medicare Appropriate Use Criteria (AUC) Program for the development of AUC and the establishment of policy and decision-making for diagnostic imaging in patients with cancer.

NCCN imposes strict policies to shield the guidelines development processes from external influences. The "firewall" surrounding the NCCN Guidelines includes financial support policies, panel participation and communication policies, guidelines disclosure policies, and policies

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For Clinicians: [NCCN.org](https://www.nccn.org) | For Patients: [NCCN.org/patients](https://www.nccn.org/patients) | Member Institutions: [NCCN.org/cancercenters](https://www.nccn.org/cancercenters)

regarding relationships to NCCN's other business development activities. The guidelines development is supported exclusively by the Member Institutions' dues and does not accept any form of industry or other external financial support for the guidelines development program. The NCCN Guidelines are updated at least annually in an evidence-based process integrated with the expert judgment of multidisciplinary panels of expert physicians from NCCN Member Institutions. The NCCN Guidelines are transparent, continuously updated, available free of charge online for non-commercial use and are available through a multitude of health information technology (HIT) vendors.

NCCN Biomarkers Compendium®

The NCCN Biomarkers Compendium® is intended to be a resource for payers, providers, and health care entities navigating the rapidly changing evidence-base for medically necessary biomarker testing in oncology. The NCCN Biomarkers Compendium® contains information derived directly from the NCCN Guidelines to support decision-making around the use of biomarker testing in patients with cancer. The NCCN Biomarkers Compendium is updated continuously in conjunction with the NCCN guidelines to stay evergreen. The goal of the NCCN Biomarkers Compendium is to provide essential details for testing methodologies which have been approved by NCCN Guideline Panels and are recommended within the NCCN Guidelines. Included in the Biomarkers Compendium are testing methodologies that measure changes in genes or gene products and used for the purposes of diagnosis, screening, monitoring, surveillance, prediction, and prognostication.

Launched in 2012 and updated in 2021 to have shared data fields with other Compendia in the Library, the information within the Biomarkers Compendium is extracted directly from Guideline algorithms, principles pages, and footnotes, and all entries are reviewed and approved by the Guideline Panel pathologist or other panel member with expertise in the area. Information within the Biomarkers Compendium focuses on the biology or abnormality being measured rather than on commercially available tests or test kits, with methodologic information provided only if included in the parent Clinical Practice Guideline.

The Biomarkers Compendium is intended to be user friendly in an easy to navigate format for payers and providers alike. The displayed fields can be customized to the user and include links to the Guideline Page on which the biomarker is addressed. Compendium entries can be printed, providing the summary of the recommendations with details regarding each field within the Compendium, in a format that is concise and easy to read. With this resource, the NCCN Biomarkers Compendium aims to ensure that patients have coverage and access to appropriate biomarker testing based on the evaluations and recommendations of NCCN Panel Members.

NCCN Guidelines and Compendia as a Tool to Keep Coverage Determinations Evergreen

Recognizing the value of continuously updated evidence-based guidelines, numerous Medicare Administrative Contractors have cited NCCN Guidelines within their proposed and final coverage

policies as a mechanism to evergreen coverage regarding drug and biologic coverage. These policies include Palmetto's Local Coverage Article: Billing and Coding: Chemotherapy (A56141) and Local Coverage Determination Luteinizing Hormone-Releasing Hormone (LHRH) Analogs (39387), Wisconsin Physician Services' LCD Chemotherapy Drugs and their Adjuncts (L37205), and National Government Services' Genomic Sequence Analysis Panels in the Treatment of Solid Organ Neoplasms (L37810) among others. NCCN is pleased to offer these guidelines and related compendia products as a resource for coverage mechanism within This would ensure the LCD stays evergreen while also significantly reducing administrative burden.

NCCN Guideline References within the LCD and Areas for Clarification

NCCN thanks CGS for referencing NCCN content within the proposed LCD. NCCN is pleased to be able to provide additional background information on these references and seeks clarification on several areas within the LCD. Specifically, NCCN notes:

- The Proposed LCD states: *“While there are a number of promising additional biomarkers, such as Ki-67, PI3K and gene expression assays, the College of American Pathologists (CAP), the American Society of Clinical Oncologists (ASCO) and the National Comprehensive Cancer Network (NCCN) have not recognized these markers in patient treatment pathways.”* NCCN respectfully notes that this aforementioned specific statement is not aligned with our guidelines. As is accurately discussed further in the LCD, the NCCN Guidelines for Breast Cancer® note on page BINV-1 that a Ki-67 test must be performed if considering adjuvant abemaciclib. PCR-based PI3KCA-mutation testing and gene expression assays are not the subject of this LCD, but determination of such biomarkers in special circumstances are noted in the NCCN Guidelines to identify candidates for alpelisib-containing regimen or to aid in prediction of response to adjuvant cytotoxic chemotherapy. NCCN respectfully requests that the above italicized statement remove the NCCN reference in the above citation and include statements to accurately reflect NCCN Guidelines recommendations as noted here.
- The LCD also states: *“Claims data indicate combinations of gram stain, PAS, Ki-67, p16 and ProExC stains on all cervical biopsies from select pathology practices, and combinations of p53, Ki-67, and CD20 and CD44 on bladder biopsies from select pathology practices.”* with a reference to the 2014 version 3 of the NCCN Guidelines for Ovarian Cancer. NCCN respectfully notes that this content is not found in either the 2014 v.3 or current (2023 v.1) NCCN Guidelines for Ovarian Cancer®. As such, NCCN requests this reference be removed.
- The LCD updates coverage criteria for IHC to state *“LS tumor screening for microsatellite instability (MSI)/DNA mismatch repair (MLH1, MSH2, MSH6 and PMS2) by qualitative IHC is considered medically necessary and covered by Medicare for individuals with newly diagnosed colorectal cancer or endometrial cancer.”*, thus removing previous age

requirements. This coverage aligns with the NCCN Clinical Practice Guidelines for Genetic/Familial High-Risk Assessment: Colorectal®.

- NCCN would like to further note several outdated versions are cited within this LCD. The NCCN Guidelines are updated on a continual basis, with a minimum of one update annually, though more frequent updates commonly occur as the science evolves. NCCN notes that the most frequent versions across our library of clinical practice guidelines can always be found online, free of charge, at NCCN.org.

NCCN again thanks CGS for including NCCN Guidelines content within the proposed LCD. NCCN appreciates the opportunity to comment on the CGS Proposed Local Coverage Determination (LCD) Special Histochemical Stains and Immunohistochemical Stains (DL35986). NCCN is happy to serve as a resource and looks forward to working together to advance access to high-quality cancer care for CGS' beneficiary population.

Sincerely,



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