National Comprehensive Cancer Network®

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November 14, 2022

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

RE: Allogeneic Hematopoietic Cell Transplantation for Primary Refractory or Relapsed Hodgkin's and Non-Hodgkin's Lymphoma with B-cell or T-cell Origin (DL39434)

Dear Dr. Loveless:

The National Comprehensive Cancer Network® (NCCN®) appreciates the opportunity to comment on the Proposed Local Coverage Determination (LCD) Allogeneic Hematopoietic Cell Transplantation for Primary Refractory or Relapsed Hodgkin's and Non-Hodgkin's Lymphoma with B-cell or T-cell Origin (DL39434) as it relates to NCCN's mission of improving and facilitating, quality, effective, equitable, and accessible cancer care. NCCN will focus our comments on areas of alignment between NCCN Guidelines® and the proposed LCD and ways NCCN content can be used as a resource to inform coverage determinations to keep LCDs evergreen as the science evolves.

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 Guidelines

NCCN develops authoritative information regarding cancer prevention, screening, diagnosis, treatment, and supportive care that is widely used by clinical professionals and payers alike. The NCCN Guidelines are a comprehensive set of 84 guidelines detailing the sequential management decisions and interventions across 218 algorithms that currently apply to 97 percent of cancers affecting patients in the United States. More than 1700 panel members participate in Guideline development. In 2021, there were 13 million downloads of the Guidelines across web-based and mobile applications. NCCN Guidelines are developed by multidisciplinary expert panels from NCCN Member Institutions in an evidence-based process integrated with expert consensus. The NCCN Guidelines are updated at least annually, but quite often are updated more frequently, with 215 total version updates across all guidelines in 2021.

The NCCN Guidelines are considered the standard for clinical care and policy in oncology in the United States. The Guidelines are the most thorough and most frequently updated clinical practice guidelines in any area of medicine, are the most frequently referenced clinical practice guideline in oncology, and are widely available free of charge for non-commercial use. Our Guidelines are also available through a multitude of health information technology vendors, used by payers representing more than 85% of covered lives in the United States, and form the basis for insurance coverage policy and quality evaluation.

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

Guideline Adherence as a Tool to Improve Outcomes, Reduce Costs, and Keep Coverage Evergreen

Numerous independent studies have found adherence to NCCN Guidelines improves care delivery and outcomes for patients with cancer. Improved health outcomes proven through concordance with NCCN Guidelines include: improved rates of survival for colon cancer, ovarian cancer, gastric

cancer, nasopharyngeal cancer, and pancreatic cancer; decreased locoregional recurrence of melanoma; and improved pain control. [1,2,3,4,5,6] .

Guideline adherent care has also been shown to decrease costs to both the payer and the patient. A peer-reviewed, published study by United, eviCore, and NCCN entitled "Transforming Prior Authorization to Decision Support" demonstrated mandatory adherence to NCCN Guidelines and NCCN Compendium® using a real-time Clinical Decision Support Mechanism by United Healthcare significantly reduced total and episodic costs of care by 20% compared to trend while also reducing denials and increasing access to guideline-concordant care.[7] A 2019 study "Guideline Discordance and Patient Cost Responsibility in Medicare Beneficiaries With Metastatic Breast Cancer" by Williams, et.al found median cost for metastatic breast cancer patients receiving guideline-discordant treatment was $7,421 versus $5,171 for those receiving guideline-concordant care.[8] This study found an additional $1,841 in out-of-pocket cost savings for patients receiving guideline concordant care versus patients who received care that did not adhere to guidelines. These cost savings have also been found in studies evaluating the Medicare population. At this year's ASCO annual conference, CVS Health presented two abstracts looking at total costs of care beginning with the first treatment and for the subsequent 180 days for breast and colon cancer patients in relation to adherence to NCCN Guidelines.[9,10] In both studies, there was a significant reduction in total cost of care with concordance with NCCN Guidelines. In the colon cancer study, this was most prominent and significant in the Medicare population. In the breast cancer study,

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1 Erickson Foster J, Velasco JM, Hieken TJ. Adverse outcomes associated with noncompliance with melanoma treatment guidelines. Annals of Surgical Oncology. 2008;15(9):2395-2402. doi:10.1245/s10434-008-0021-0

2 Visser BC, Ma Y, Zak Y, Poultsides GA, Norton JA, Rhoads KF. Failure to comply with NCCN guidelines for the management of pancreatic cancer compromises outcomes. HPB. 2012;14(8):539-547. doi:10.1111/j.1477-2574.2012.00496.x

3 Bristow RE, Powell MA, Al-Hammadi N, et al. Disparities in ovarian cancer care quality and survival according to race and socioeconomic status. JNCI Journal of the National Cancer Institute. 2013;105(11):823-832. doi:10.1093/jnci/djt065

4 Bristow RE, Chang J, Ziogas A, Randall LM, Anton-Culver H. High-volume ovarian cancer care: Survival impact and disparities in access for advanced-stage disease. Gynecologic Oncology. 2014;132(2):403-410. doi:10.1016/j.ygyno.2013.12.017

5 Mearis M, Shega JW, Knoebel RW. Does adherence to National Comprehensive Cancer Network guidelines improve pain-related outcomes? An Evaluation of Inpatient Cancer Pain Management at an Academic Medical Center. Journal of Pain and Symptom Management. 2014;48(3):451-458. doi:10.1016/j.jpainsymman.2013.09.016

6 Schwam ZG, Sosa JA, Roman S, Judson BL. Receipt of care discordant with practice guidelines is associated with compromised overall survival in nasopharyngeal carcinoma. Clinical oncology (Royal College of Radiologists (Great Britain)). https://www.ncbi.nlm.nih.gov/pubmed/26868285. Published June 2016.

7. Newcomer LN, Weininger R, Carlson RW. Transforming prior authorization to decision support. Journal of Oncology Practice. 2017;13(1). doi:10.1200/jop.2016.015198

8 Williams CP, Azuero A, Kenzik KM, et al. Guideline discordance and patient cost responsibility in medicare beneficiaries with metastatic breast cancer. *Journal of the National Comprehensive Cancer Network*. 2019;17(10):1221-1228. doi:10.6004/jnccn.2019.7316

9 Sapkota U, Cavers W, Reddy S, Avalos-Reyes E, Johnson KA. Total cost of care differences in National Comprehensive Cancer Center (NCCN) concordant and non-concordant breast cancer patients. *JCO*. 2022;40(16_suppl):e18833-e18833. doi:10.1200/JCO.2022.40.16_suppl.e18833

10 Sapkota U, Cavers W, Reddy S, Avalos-Reyes E, Johnson KA. Total cost of care differences in National Comprehensive Cancer Center (NCCN) concordant and non-concordant patients with colon cancer. *JCO*. 2022;40(16_suppl):3624-3624. doi:10.1200/JCO.2022.40.16_suppl.3624

significant reductions were observed across both commercially insured and Medicare patients, with the greatest reductions again seen in the Medicare population.

Nationally Recognized Guidelines as an Evergreening Mechanism for Coverage Determination

Public and commercial payers employ NCCN Guidelines within their coverage mechanisms to ensure evergreening of coverage while also reducing administrative burden. As noted above, adherence to NCCN Guidelines has been proven to improve quality across a variety of outcome measures, reduce costs to the payer and health care system, and reduce costs to the patient. The 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 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.

Recognizing the value of continuously updated evidence-based guidelines, numerous Medicare Administrative Contractors have cited NCCN Guidelines within their coverage policies as a mechanism to evergreen coverage. Relevant policies include Palmetto's Local Coverage Article: Billing and Coding: Chemotherapy (A56141), 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 recommends that CGS consider the incorporation of nationally recognized guidelines into the proposed LCD coverage indications to ensure the LCD stays evergreen while also significantly reducing administrative burden.

NCCN Guideline Recommendations of Relevance to the Proposed LCD

Within the proposed LCD, CGS proposes to cover allogenic hematopoietic cell transplant when:

1. *Patient has primary refractory or relapse of Hodgkin's or non-Hodgkin's lymphoma with B-cell or T-cell origin*
2. *Pre-transplantation assessment indicates good function status, low-comorbidities and patient is candidate for transplantation based on risk assessment*
3. *There are no other treatment options available with curative intent*

The NCCN Guidelines for B-Cell Lymphomas and NCCN Guidelines for T-Cell Lymphomas recommend allogeneic hematopoietic transplantation (HCT) as an option for patients with relapsed/refractory disease who achieve a response to second-line therapy. NCCN Guidelines for B-Cell Lymphomas recommend consideration of allogeneic HCT in selected patients (those with stem mobilization failures and those with persistent disease in the bone marrow are not candidates for

autologous HCT) who have achieved either a complete response (CR) or a partial response (PR) to second-line therapy and have chemosensitive disease at the time of transplant. However, allogeneic HCT is not recommended for patients with primary refractory disease (i.e. patients with disease that has never achieved a CR from any therapy and also for patients who are not in PR at the time of the last evaluation prior to HCT). In general, the presence of refractory disease at the time of transplant is considered a poor prognostic factor and outcomes following allogeneic HCT are also very poor in patients with primary refractory disease. CAR T-cell therapy is the recommended treatment option for patients with primary refractory disease (i.e. primary refractory diffuse large B-cell lymphoma [DLBCL]) in the NCCN Guidelines for B-Cell Lymphomas.

NCCN appreciates the opportunity to comment on the Proposed Local Coverage Determination Allogeneic Hematopoietic Cell Transplantation for Primary Refractory or Relapsed Hodgkin's and Non-Hodgkin's Lymphoma with B-cell or T-cell Origin (DL39434). NCCN again encourages CGS to consider NCCN as a resource for Local Coverage Determinations. We look forward to working together to ensure Medicare beneficiary access to high-quality cancer care.

Sincerely,

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