Drug Policy:

Criteria for Evidence-Based Cancer Therapies

POLICY NUMBER UM ONC_1209	**SUBJECT** Criteria for Evidence-Based Cancer Therapies		**DEPT/PROGRAM** UM Dept	**PAGE 1 OF 6**
DATES COMMITTEE REVIEWED 05/09/12, 05/17/12, 07/06/12, 06/01/13, 07/24/14, 12/15/15, 01/11/17, 01/10/18, 01/08/19, 12/11/19, 01/08/20, 11/11/20, 11/10/21, 09/14/22, 02/08/23, 02/14/24	**APPROVAL DATE** February 14, 2024	**EFFECTIVE DATE** February 23, 2024	**COMMITTEE APPROVAL DATES** 05/09/12, 05/17/12, 07/06/12, 06/01/13, 07/24/14, 12/15/15, 01/11/17, 01/10/18, 01/08/19, 12/11/19, 01/08/20, 11/11/20, 11/10/21, 09/14/22, 02/08/23, 02/14/24	
PRIMARY BUSINESS OWNER: UM		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee		
NCQA STANDARDS UM 2		**ADDITIONAL AREAS OF IMPACT**		
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** Commercial, Exchange, Medicaid	

I. PURPOSE

To define the processes to ensure the use of evidence-based cancer therapies with high effectiveness and level of evidence to improve health outcomes and overall quality cancer care to all patients.

II. DEFINITIONS

Evidence-based Medicine: Decision making tools that are based on the integration of clinically relevant research, expert opinion, and current standards of care. This guideline provides a purposeful and clear evaluation of the effectiveness of diagnostic and/or therapeutic modalities. Effectiveness is defined as a measure of the benefit resulting from an intervention for a given health problem under average conditions of use.

Off-Label Supported Drug Use: The use of a drug that deviates from the labeled prescribing information for a particular indication. The use is supported by clinical research and is published in any of the major compendia, authoritative medical literatures and/or accepted standards of medical practice.

Peer-reviewed Medical Literature: Original manuscripts that are published in scientific, medical, and pharmaceutical publications after having been critically reviewed for scientific accuracy, validity, and reliability by unbiased, independent experts prior to publication.

Compendium: A comprehensive listing of FDA-approved drugs and biological or a comprehensive listing of a specific subset of drugs and biological in a specialty compendium. An approved compendium: (1) includes a summary of the pharmacologic characteristics of each drug or biologic and may include information on dosage, as well as recommended or endorsed uses in specific

diseases; (2) is indexed by drug or biologic, and (3) has a publicly transparent process for evaluating therapies and for identifying potential conflicts of interests.

National Coverage Determination (NCD) or Local Coverage Determination (LCD): A nationwide or local determination of whether Medicare will pay for an item or service.

National Comprehensive Cancer Network (NCCN) Categories of Evidence and Consensus:
Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Evidence-based Cancer Therapy: A single agent or combination of chemotherapeutic agents recommended based on the level of supporting evidence and is given for a targeted patient population with a specific type of cancer at the right dose, route, duration and frequency of administration, and clinical stage of the disease.

III. POLICY

Evolent's determination of the evidence-based cancer therapies shall rely on the strength of evidence and the assessment of efficacy, toxicity, and cost as evaluated by Evolent Medical Oncology Policy Committees and/or the Oncology Scientific Advisory Board. Evolent may rely on additional support from compendia such as the NCCN compendium or support from another approved compendium and/or peer reviewed clinical literature. The evidence-based cancer therapy shall be preferred as front-line therapy to enhance the most cost-effective therapeutic option while still promoting the desired clinical outcome and safety.

IV. PROCEDURE

A. When evaluating and weighing the grading of the evidence, the following evidence-based criteria are considered:
    1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
    2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
    3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
    4. Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover)

5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

B. When evaluating the criteria to determine the evidenced-based cancer therapy, the following desirable conditions are met:
   1. That the process of research and evaluation of the evidence for a recommended preferred cancer therapy include input from a rigorous internal review team of oncology specialists and is free of any potential conflicts of interests.
   2. That the use of evidentiary materials or references include the desired evidenced-based characteristics, in most cases, the highest level of evidence, safety, and efficacy are considered for inclusion (see inclusion/exclusion criteria below)
   3. That the criteria meet the needs of the patient population.
   4. That Evolent UM committee review and approve the criteria at least annually and update as appropriate.

C. The evidence-based cancer therapies may be defined by any of the following criteria:
   1. Criteria for Level 1 Pathways: A subset of cancer therapies that have the highest levels of evidence supporting their effectiveness, least toxicity, and all factors being equal, the lowest cost,
   2. Criteria for Level 2 Pathways: A subset of cancer therapies that are supported by CMS approved compendia, accepted peer review literature, and/or national clinical practice guidelines (e.g., NCCN, ASCO).
   3. Criteria for Low Value Regimens: A subset of cancer therapies characterized by one or more of the following:
      a. No clinically meaningful survival advantage and/or impaired QOL versus available alternatives.
      b. Accelerated approvals using surrogate endpoints and serving no unmet need.
      c. Excessive toxicities compared to available alternatives.
      d. Excessive cost compared to available alternatives.

V. INCLUSION CRITERIA

A. The on-label or off-label use of the evidence-based cancer therapy is a medically accepted indication supported by any ONE of the following:
   1. Peer-reviewed literature: Limited to Level 1 evidence (as defined by the Oxford Centre for Evidence Based Medicine) phase III randomized controlled trials and/or systematic reviews/meta-analyses. Published phase II studies will be considered for determination of medical necessity on a case by case basis.
   2. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
      a. Indication is a Category 1 based upon high-level evidence and uniform NCCN consensus that the intervention is appropriate.
      b. Indication is a Category 2A based upon lower-level evidence and uniform NCCN consensus that the intervention is appropriate.

3. Micromedex Drugdex
    a. Indication is a Class 1: recommended, the given treatment has been proven to be useful, and should be performed or administered.
    b. Indication is a Class IIa: recommended in most cases, the given treatment is generally considered to be useful and is indicated in most cases.
    c. Indication is a Class IIb: recommended in some cases, the given treatment may be useful and is indicated in some but not most cases.
4. Clinical Pharmacology Elsevier Gold Standard
    a. The quality of evidence rating is moderate or high AND the strength of the recommendation is strong AND
    b. The listed indication is supported by a narrative text.
5. American Hospital Formulary Service-Drug Information (AHFS-DI)
    a. The quality of evidence rating is moderate or high AND the strength of the recommendation is:
        i. ACCEPTED: the drug or biologic should be used, is recommended/indicated, or is useful/effective/beneficial in most cases OR
        ii. ACCEPTED with possible conditions: the drug or biologic is reasonable to use under certain conditions, can be useful/effective/beneficial, or is probably recommended or indicated.
        iii. The listed indication is supported by a narrative text.
6. Wolters Kluwer Lexi-Drugs
    a. Indication is listed as evidence Level A.
    b. The listed indication is supported by a narrative text.

B. Peer Reviewed Medical Literature
1. The evidence-based cancer therapy is being used for an indication outside the approved FDA manufacturer labeling or the approved drug compendia. As such, the indication must be supported by clinical research and is published in one of the following peer-reviewed medical journals.

    American Journal of Medicine

    Annals of Internal Medicine

    Annals of Oncology

    Annals of Surgical Oncology

    Biology of Blood and Marrow Transplantation

    Blood

    Bone Marrow Transplantation

    British Journal of Cancer

    British Journal of Hematology

    British Medical Journal

    Cancer

    Clinical Cancer Research

    Drugs

European Journal of Cancer (formerly the European Journal of Cancer and Clinical Oncology)

Gynecologic Oncology

International Journal of Radiation, Oncology, Biology, and Physics

The Journal of the American Medical Association

Journal of Clinical Oncology

Journal of the National Cancer Institute

Journal of the National Comprehensive Cancer Network (NCCN)

Journal of Urology

Lancet

Lancet Oncology

Leukemia

The New England Journal of Medicine

Radiation Oncology

VI. EXCLUSION CRITERIA

A. Off Label Use (Not Supported by Evidence): The cancer therapy is being used for an indication that is listed as unsupported, not indicated, not recommended, or equivalent terms in any ONE of the following:
   1. FDA manufacturer label
   2. Peer-reviewed literature
   3. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
      a. Category 2B indication that is based upon lower-level evidence and there is NCCN consensus that the intervention is appropriate.
      b. Category 3 indication that is based upon any level of evidence and there is major NCCN disagreement that the intervention is appropriate.
   4. Micromedex Drugdex Class III indication that is not recommended, and the given treatment is not useful and should be avoided.
   5. Clinical Pharmacology Elsevier Gold Standard listed indication has a low or very low evidence rating AND equivocal or weak recommendation.
   6. American Hospital Formulary Service-Drug Information (AHFS-DI) or Wolters Kluwer Lexi-Drugs indication has a:
      a. Low evidence rating evidence consists of observational studies, case reports or case series or randomized clinical trials with multiple serious deficiencies or study limitations OR
      b. Recommendation that is not fully established with unclear risk/benefit, equivocal evidence, inadequate data and or experience.
      c. Indication is listed as Use: “Unsupported” or “Not Supportive”.

B. The cancer therapy is being used for an indication listed without a supported narrative text in Clinical Pharmacology, AHFS-DI, or Wolters Kluwer Lexi-Drugs

C. The cancer therapy is being used for an indication listed in one of the following published literature:

1. Abstracts (including meeting abstracts)
2. Supplement editions of peer-reviewed medical literature that is privately funded by parties with vested interest in the recommendations of the authors
3. Case reports.

VII. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VIII. ATTACHMENTS

A. None

IX. REFERENCES

A. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2023.

B. Clinical Pharmacology Elsevier Gold Standard. 2023.

C. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2023.

D. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2023.

E. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.

F. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.