Evolent Clinical Guideline 3080 for Doxil™ (liposomal doxorubicin)

Guideline Number:	Applicable Codes	
Evolent_CG_3080		
"Evolent" refers to Evolent Health LLC and Evolent Specialty Services, Inc. 		
Original Date:	**Last Revised Date:**	**Implementation Date:**
December 2012	May 2025	May 2025

TABLE OF CONTENTS

STATEMENT **2**
PURPOSE 2
INDICATIONS **2**
AIDS-RELATED KAPOSI'S SARCOMA (KS) 2
BREAST CANCER 2
HODGKIN LYMPHOMA 2
MULTIPLE MYELOMA 2
OVARIAN CANCER 3
CONTRAINDICATIONS/WARNINGS **3**
EXCLUSION CRITERIA **3**
CODING AND STANDARDS **4**
CODES 4
APPLICABLE LINES OF BUSINESS 4
POLICY HISTORY **5**
LEGAL AND COMPLIANCE **5**
GUIDELINE APPROVAL 5
Committee *5*
DISCLAIMER 5
REFERENCES **6**

STATEMENT

Purpose

To define and describe the accepted indications for Doxil (liposomal doxorubicin) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

INDICATIONS

Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

AIDS-related Kaposi's Sarcoma (KS)

- Doxil (liposomal doxorubicin) will be used for the treatment of AIDS-related Kaposi's sarcoma as a single agent or in combination with antiretroviral therapy, as initial or subsequent line systemic therapy.

Breast Cancer

- NOTE: Doxil (liposomal doxorubicin) is not supported by Evolent Policy for the treatment of recurrent, unresectable, or metastatic breast cancer. This policy position is based on the lack of Level 1 Evidence (randomized clinical trial and/or meta-analyses) to show superior outcomes with Doxil (liposomal doxorubicin) compared to conventional formulation of doxorubicin (e.g., Adriamycin). Please refer to Evolent alternative agents/regimens recommended by Evolent, including but not limited to regimens available at **Evolent Pathways**.

Hodgkin Lymphoma

- Doxil (liposomal doxorubicin) may be used in combination with gemcitabine and vinorelbine as second-line and subsequent therapy in members with relapsed or refractory Hodgkin Lymphoma.

Multiple Myeloma

- The member has relapsed or refractory multiple myeloma and Doxil (liposomal

doxorubicin) will be used in combination with bortezomib (if have not previously received) +/- dexamethasone following one prior therapy.

Ovarian Cancer

- Doxil (liposomal doxorubicin) will be used in combination with carboplatin for platinum sensitive relapsed/recurrent ovarian cancer OR
- As a single agent or in combination with bevacizumab/bevacizumab biosimilar for platinum-resistant relapsed/recurrent ovarian cancer.

CONTRAINDICATIONS/WARNINGS

- Contraindications
  - History of severe hypersensitivity (including anaphylaxis) to liposomal doxorubicin, conventional doxorubicin, or any component of the formulation.
- US Boxed Warning
  - Cardiomyopathy
    - Liposomal doxorubicin can cause myocardial damage, including acute left ventricular failure. The risk of cardiomyopathy was 11% when the cumulative anthracycline dose was between 450 and 550 mg/m^2. Assess left ventricular cardiac function prior to initiation of liposomal doxorubicin, and during and after treatment.
  - Infusion-related reactions
    - Serious, life-threatening, and fatal infusion-related reactions can occur with liposomal doxorubicin. Acute infusion-related reactions occurred in 11% of patients with solid tumors. Withhold liposomal doxorubicin for infusion-related reactions and resume at a reduced rate. Discontinue liposomal doxorubicin for serious or life-threatening infusion-related reactions.

EXCLUSION CRITERIA

- Disease progression while taking Doxil (liposomal doxorubicin).
- Dosing exceeds single dose limit of Doxil (liposomal doxorubicin) 50 mg/m^2 (for ovarian cancer), 20 mg/m^2 (for KS), 30 mg/m^2 (for multiple myeloma), and 15 mg/m2 (for Hodgkin Lymphoma).
- Investigational use of Doxil (liposomal doxorubicin) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
  - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
  - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.

- 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.
- 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).
- 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.
- That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
- 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.

CODING AND STANDARDS

Codes

- Q2050 - Injection, doxorubicin hydrochloride, liposomal, not otherwise specified, 10 mg

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
May 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1235 Doxil (liposomal doxorubicin) • Updated references
May 2024	• Added Hodgkin Lymphoma indication for use in combination with gemcitabine and vinorelbine as second-line and subsequent therapy in members with relapsed or refractory Hodgkin Lymphoma • Added new reference • Updated exclusion criteria

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

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