

Medical Drug Clinical Criteria

Subject: Doxorubicin Liposome (Doxil)

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Overview

This document addresses the use of doxorubicin liposome (Doxil). Doxorubicin liposome is a cytotoxic, anthracycline topoisomerase II inhibitor used in the treatment of oncologic conditions.

The FDA approved indications for doxorubicin liposome are advanced ovarian cancer, AIDS-related Kaposi's sarcoma, and multiple myeloma. The National Comprehensive Cancer Network (NCCN) provides additional recommendations with a category 2A level of evidence for the use of breast cancer, B and T cell lymphomas including Hodgkin's lymphoma and Non-Hodgkin's lymphoma including both indolent and aggressive forms of NHL (e.g. mycosis fungoides and Sézary syndrome), advanced soft tissue sarcoma, and advanced or recurrent uterine neoplasms.

There is a black box warning with doxorubicin liposome for cardiomyopathy (including congestive heart failure) and infusion-related reactions consisting of, but not limited to, flushing, shortness of breath, facial swelling, headache, chills, back pain, tightness in the chest or throat, and/or hypotension.

Definitions and Measures

Chemotherapy: Medical treatment of a disease, particularly cancer, with drugs or other chemicals.

Complete Response (CR): The disappearance of all signs of cancer as a result of treatment; also called complete remission; does not indicate the cancer has been cured.

Cytotoxic: Treatment that is destructive to cells, preventing their reproduction or growth.

Line of Therapy:

- **First-line therapy:** The first or primary treatment for the diagnosis, which may include surgery, chemotherapy, radiation therapy or a combination of these therapies.
- **Second-line therapy:** Treatment given when initial treatment (first-line therapy) is not effective or there is disease progression.
- **Third-line therapy:** Treatment given when both initial (first-line therapy) and subsequent treatment (second-line therapy) are not effective or there is disease progression.

Off-Label: Utilization of an FDA approved drug for uses other than those listed in the FDA approved label.

Partial response (PR): A decrease in the size of a tumor, or in the amount of cancer in the body, resulting from treatment; also called partial remission.

Platinum-resistant: Disease reoccurs in less than six months after receiving platinum based chemotherapy.

Platinum-sensitive: Disease relapses after six months or more after receiving platinum based chemotherapy.

Progressive Disease (PD): Cancer that is growing, spreading, or getting worse.

Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

Stable disease: Cancer that is not decreasing or increasing in extent or severity.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Doxorubicin Liposome (Doxil)

Requests for Doxorubicin Liposome (Doxil) may be approved if the following criteria are met:

- I. Individual has a diagnosis of *one* of the following:
 - A. Breast cancer when used as monotherapy for recurrent or metastatic disease (NCCN 2A); **OR**
 - B. Kaposi's sarcoma, AIDS-related; **OR**
 - C. Hodgkin's Lymphoma (e.g. classical Hodgkin lymphoma or nodular lymphocytic predominant Hodgkin lymphoma) when used as a second-line or subsequent therapy for refractory or relapsed disease (NCCN 2A); **OR**
 - D. Non-Hodgkin lymphoma (NCCN 2A); **OR**
 - E. Multiple myeloma when agent used as second-line or later line of therapy; **OR**
- F. Ovarian cancer (including epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer) that is **persistent or recurrent disease** when *one* of the following is met:
 1. Agent used as monotherapy; **OR**
 2. Agent used in combination with carboplatin (NCCN 1, 2A); **OR**
 3. Agent used in combination with bevacizumab, if bevacizumab (bevacizumab biosimilar), was not previously used for treatment of ovarian cancer (NCCN 2A); **OR**
 4. Agent used in combination with carboplatin and bevacizumab (or bevacizumab biosimilar), if bevacizumab was not previously used for treatment of ovarian cancer (NCCN 1, 2A); **OR**
- G. Sarcomas, soft tissue when *one* of the following is met (NCCN 2A):
 1. Angiosarcoma when used as a monotherapy; **OR**
 2. **Dermatofibrosarcoma protuberans (DFSP) with fibrosarcomatous transformation used as monotherapy; OR**
 3. **Dedifferentiated chordoma used as monotherapy; OR**
 - 2-4. Desmoid tumors; **OR**
 - 3-5. Retroperitoneal/intra-abdominal sarcomas when used as monotherapy; **OR**
 - 4-6. Rhabdomyosarcoma when used as monotherapy; **OR**
 - 6-7. Soft tissue sarcoma of the extremity, superficial trunk, head or neck when used as monotherapy; **OR**
 - 6-8. Solitary fibrous tumor when used as monotherapy; **OR**
- H. Uterine neoplasm when *one* of the following is met (NCCN 2A):
 1. Endometrial carcinoma when used as monotherapy; **OR**
 2. Uterine sarcoma when used as monotherapy for advanced or metastatic disease.

Doxorubicin Liposome (Doxil) may not be approved when the above criteria are not met and for all other indications.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

Q2049	Injection, doxorubicin hydrochloride, liposomal, imported lipodox, 10 mg
Q2050	Injection, doxorubicin hydrochloride, liposomal, not otherwise specified, 10 mg [Doxil]

ICD-10 Diagnosis

B20	Human immunodeficiency virus [HIV] disease
C44.09	Other specified malignant neoplasm of skin of lip [dermatofibrosarcoma protuberans]
C44.191-C44.199	Other specified malignant neoplasm of skin of eyelid, including canthus
C44.291-C44.299	Other specified malignant neoplasm of skin of ear and external auricular canal
C44.390-C44.399	Other specified malignant neoplasm of skin of other and unspecified parts of face
C44.49	Other specified malignant neoplasm of skin of scalp and neck
C44.590-C44.599	Other specified malignant neoplasm of skin of trunk

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C44.691-C44.699	Other specified malignant neoplasm of skin of upper limb, including shoulder
C44.791-C44.799	Other specified malignant neoplasm of skin of lower limb, including hip
C44.89	Other specified malignant neoplasm of overlapping sites of skin
C44.99	Other specified malignant neoplasm of skin, unspecified
C46.0-C46.9	Kaposi's sarcoma
C48.0-C48.8	Malignant neoplasm of retroperitoneum and peritoneum
C50.011-C50.929	Malignant neoplasm of breast
C54.0-C55	Malignant neoplasm of corpus uteri, uterus part unspecified
C56.1-C56.9	Malignant neoplasm of ovary
C57.00-C57.9	Malignant neoplasm of other and unspecified female genital organs
C79.81	Secondary malignant neoplasm breast
C81.00-C81.99	Hodgkin lymphoma
C83.00-C83.09	Small cell B-cell lymphoma
C83.30-C83.39	Diffuse large B-cell lymphoma
C83.80-C83.99	Other non-follicular lymphoma, non-follicular (diffuse) lymphoma, unspecified
C84.00-C84.19	Mycosis fungoides, Sézary disease
C84.40-C84.49	Peripheral T-cell lymphoma, not classified
C84.60-C84.79	Anaplastic large cell lymphoma
C84.A0-C84.A9	Cutaneous T-cell lymphoma, unspecified
C84.Z0-C86.6	Other mature T-NK cell lymphomas, other specified and unspecified types of non-Hodgkin lymphoma,
C88.4	Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue [MALT-lymphoma]
C90.00-C90.32	Multiple myeloma
D47.Z2	Castleman disease
D48.1	Neoplasm of uncertain behavior of connective and other soft tissue [desmoid tumor]
L90.5	Scar conditions and fibrosis of skin
Z85.3	Personal history of malignant neoplasm of breast
Z85.43	Personal history of malignant neoplasm of ovary
Z85.71	Personal history of Hodgkin lymphoma

Document History

Revised: 05/19/2023

Document History:

- 05/19/2023 – Annual Review: edit ovarian cancer criteria, add DFSP and Dedifferentiated chordoma sarcoma subtype. Coding Reviewed: No changes. 05/20/2022 – Annual Review: No changes. Coding Reviewed: No changes.
- 05/21/2021 – Annual Review: Update criteria to add use for solitary fibrous tumor per NCCN. Remove obsolete agent Lipodox. Coding Review: Added ICD-10-CM L90.5.
- 05/15/2020 – Annual Review: Remove approvable criteria for non-melanoma dermatofibrosarcoma protuberans metastatic disease per NCCN update. Update Doxil use in ovarian cancer to remove combination use with cisplatin, and add approvable criteria for use with carboplatin and bevacizumab per NCCN. Add biosimilar language for bevacizumab. Wording and formatting updates for consistency. Coding reviewed: Removed ICD-10-Dx C49.0-C49.9
- 05/17/2019 – Annual Review: Initial review of doxorubicin liposome. Minor wording and formatting updates. Coding reviewed. No changes.

References

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 - b. Breast cancer V2.2022. Revised December 20, 2021.
 - c. Hodgkin Lymphoma V2.2022. Revised February 23, 2022.
 - d. Kaposi Sarcoma V1.2022. Revised February 3, 2022.
 - e. Multiple myeloma V5.2022. Revised March 9, 2022.
 - f. Ovarian cancer V1.2023. Revised December 22, 2022.
 - g. Primary Cutaneous Lymphomas V1.2022. Revised January 26, 2022.
 - h. Soft tissue sarcoma V1.2022. Revised March 29, 2022.
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