Medical Policy:
Liposomal Doxorubicin (Doxil®/Lipodox®)

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.142	February 2, 2024	

Definitions

Doxil®/Lipodox® (liposomal doxorubicin): Doxorubicin is an anthracycline topoisomerase inhibitor isolated from Streptomyces peucetius var. caesius. Doxorubicin is the active cytotoxic agent in Doxorubicin Liposomal. The mechanism of action of doxorubicin HCl is thought to be related to its ability to bind DNA and inhibit nucleic acid synthesis. Cell structure studies have demonstrated rapid cell penetration and perinuclear chromatin binding, rapid inhibition of mitotic activity and nucleic acid synthesis, and induction of mutagenesis and chromosomal aberrations.

Doxil/Lipodox (liposomal doxorubicin) is FDA approved for the treatment of:

- AIDS-related Kaposi's sarcoma, In patients that have progressed or are intolerant to other combination chemotherapy regimens
- Multiple myeloma, In combination with bortezomib in patients who have not received bortezomib and have received at least one prior therapy
- Ovarian carcinoma, In patients whose disease has progressed or recurred after platinum-based chemotherapy

Non-FDA approved indications include:

- Breast Cancer
- Endometrial Cancer
- Hodgkin Lymphoma
- Soft Tissue Sarcoma
- T-cell or B-cell Lymphomas

Length of Authorization

Coverage will be provided for 6 months and may be renewed.

Guideline

I. Initial Approval Criteria

Doxil®/Lipodox® (liposomal doxorubicin) *may be considered medically necessary if one of the below conditions are met **AND** use is consistent with the medical necessity criteria that follows:*

1. **AIDS Related Kaposi's Sarcoma (KS)**
    A. For the treatment of HIV-related Kaposi's sarcoma in members with disease that has progressed on prior combination chemotherapy or in patients who are intolerant to other therapy.
2. **Multiple Myeloma**
    A. For the treatment of relapsed or refractory multiple myeloma and Doxil/Lipodox (liposomal doxorubicin) is being used in combination with bortezomib in patients who have received at least 1 prior therapy and is bortizomib naïve.
3. **Ovarian Cancer**
    A. Doxil/Lipodox (liposomal doxorubicin) is being used for the treatment of ovarian cancer that has progressed or recurred for the **ONE** of the following:
        i. After platinum-based chemotherapy as a single agent or in combination with bevacizumab if bevacizumab not previously received .
        ii. If platinum sensitive, in combination with carboplatin for persistent disease or recurrence.
4. **Breast Cancer**
5. **Endometrial Carcinoma**
6. **Hodgkin Lymphoma**
7. **Soft Tissue Sarcoma**
8. **T-cell or B-cell Lymphomas**

Limitations/Exclusions

Doxil/Lipodox (liposomal doxorubicin) is not considered medically necessary when any of the following selection criteria is met:

1. Disease progression while taking Doxil/Lipodox (liposomal doxorubicin).
2. History of severe hypersensitivity reactions, including anaphylaxis, to standard doxorubicin (Adriamycin).
3. Concurrent use with another anthracycline.
4. Dosing exceeds single dose limit of Doxil/Lipodox (liposomal doxorubicin) 50 mg/m^2.
5. Dosing exceeds the total cumulative doses of 550 mg/m^2.
6. Members who have not progress after initial treatment of their KS, multiple myeloma or ovarian cancer.
7. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

II. Renewal Criteria

Authorizations may be renewed provided the patient continues to meet criteria in INITIAL APPROVAL CRITERIA.

Dosage/Administration

Indication	Dose
AIDS related Kaposi's Sarcoma (KS)	20 mg/m^2 (doxorubicin equivalent) once every 2 to 3 weeks. Therapy should be continued for as long as patients remain responsive and tolerate the drug.
Multiple Myeloma	30 mg/m^2 IV infusion on DAY 4 ONLY. Cycles are repeated every 3 weeks until disease progression or unacceptable toxicity, for up to 8 cycles.
Ovarian Cancer, Soft Tissue Sarcoma, Uterine Cancer, Breast Cancer	50 mg/m^2 administered ONCE every 4 weeks as long as the tumor does NOT progress and the patient tolerates treatment.
B-Cell and T-Cell Lymphomas	Administer 30 mg/m^2 given intravenously every 3 weeks for 6 to 8 cycles

Applicable Procedure Codes

Code	Description
Q2049	Injection, doxorubicin hydrochloride, liposome, Lipodox, 10 mg, 1 billable unit = 10 mg
Q2050	Injection, doxorubicin hydrochloride, liposome, Doxil, 10 mg, 1 billable unit = 10 mg

Applicable NDCs

Code	Description
00338-0063-xx	Doxil 20mg/10mL
00338-0067-xx	Doxil 50mg/25mL
47335-0082-xx	Lipodox 20 mg/ 10mL
47335-0083-xx	Lipodox 50mg/25mL

ICD-10 Diagnoses

Code	Description
C22.3	Angiosarcoma of liver
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
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

C49.0-C49.9	Malignant neoplasm of other connective and soft tissue
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]
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
Z85.79	Personal history of other malignant neoplasm of lymphoid hematopoietic and related tissues
Z85.831	Personal history of malignant neoplasm of soft tissue

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	2/2/2024	Annual Review: Updated dosing chart, no criteria changes
EmblemHealth & ConnectiCare	6/12/2023	Annual Review: Removed Non-Hodgkin's Lymphoma and criteria; added T-cell and B-cell Lymphomas indication (non-FDA approved); Breast Cancer: removed criteria" a. Preferred single agent for patients with recurrent or metastatic disease that is: i. hormone receptor-positive, human epidermal growth factor receptor 2 (HER2)- negative with visceral crisis ii.HER2-negative and either hormone receptor-negative or hormone receptor-positive and endocrine therapy refractory iii. progressive with no clinical benefit after three consecutive endocrine therapy regimens or with symptomatic visceral disease." Endometrial Carcinoma: removed criteria: "a.Primary treatment as a single agent i. With sequential radiation therapy (RT) and brachytherapy with or without surgery for extrauterine pelvic disease ii. Consider following palliative hysterectomy with bilateral salpingo-oophorectomy with or without RT and hormonal therapy for extra-abdominal or liver disease.

		b. Completely surgically staged patients as a single agent i. With or without sequential tumor-directed RT for stage IIIA, IIIB, and IIIC disease ii. With or without sequential RT for stage IV disease. c. Single agent i. For low-grade or asymptomatic disseminated metastases that have progressed on hormonal therapy ii. With or without sequential palliative radiation therapy (RT) for symptomatic, grade 2-3, or large volume metastases iii. With sequential tumor-directed RT with or without brachytherapy for local recurrence in patients with disease confined to the vagina or in pelvic, para-aortic, or common iliac lymph nodes iv. With or without sequential tumor-directed RT for microscopic upper abdominal or peritoneal recurrences v. For local/regional recurrence in patients who have received prior external beam RT to site of recurrence. d. Adjuvant therapy as a single agent with or without sequential tumor-directed radiation therapy" Hodgkin Lymphoma: removed Criteria: "a. Second-line or salvage therapy as a component of GVD (gemcitabine, vinorelbine, and liposomal doxorubicin) regimen prior to autologous stem cell rescue for progressive disease or for relapsed disease in patients initially treated with chemotherapy." Soft Tissue Sarcoma: removed Criteria: "a.As a single agent for preoperative, adjuvant, unresectable, recurrent , or metastatic soft tissue sarcoma of the extremity/trunk or retroperitoneal/intraabdominal origins." Removed NDC: 59676-0960-xx, added NDCs: 00338-0063-xx, 00338-0067-xx, and 47335-0083-xx. Removed ICD-10 Codes: B20, Added ICD-10 Codes: C22.3, Z85.79, Z85.831
EmblemHealth & ConnectiCare	09/06/2022	Transferred policy to new template
EmblemHealth & ConnectiCare	07/15/2019	Annual review

References

1. Doxil prescribing information. Janssen Products, LP Horsham, PA 2016.
2. Clinical Pharmacology Elsevier Gold Standard. 2016.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2016.
4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2016
5. AHFS Drug Information. American Society of Health-Systems Pharmacists. Bethesda, MD. 2016.