



**Doxorubicin (Doxil®)**  
**Revision: 3**

**Policy Number: M-0021**  
**Updated: 6/4/2014**

Payment will not be made for any use of these drugs outside of the criteria without prior authorization. The member may not be billed unless the member explicitly agrees in writing to be responsible for the charges in accordance with the contract/provider manual. Prior authorization will only be given if the provider demonstrates the intended use meets Medicare coverage guidelines.

When appropriate compendia references the use of one of the chemotherapeutic agents listed in this Article as part of a 'combination therapy', the drug is only approved for use in such 'combinations', and the documentation should reflect, and be specific about, the use of the additional 'combination therapy' drugs.

#### **Coverage Guidelines:**

##### **FDA:**

- 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

##### **Off Label:**

- Breast cancer, Locally advanced or metastatic
- Multiple myeloma, In combination with vincristine, dexamethasone, and thalidomide
- Multiple myeloma, In combination with vincristine and dexamethasone



**Coding Information:**

HCPCS Code(s)

Q2049	INJECTION, DOXORUBICIN HYDROCHLORIDE, LIPOSOMAL, IMPORTED LIPODOX, 10 MG
Q2050	INJECTION. DOXORUBICIN, HYDROCHLORIDE, LIPOSOMAL, NOT OTHERWISE SPECIFIED, 10MG

ICD-9 Code(s)

158.8	MALIGNANT NEOPLASM OF SPECIFIED PARTS OF PERITONEUM
174.0-175.9	MALIGNANT NEOPLASM OF NIPPLE AND AREOLA OF FEMALE BREAST - MALIGNANT NEOPLASM OF OTHER AND UNSPECIFIED SITES OF MALE BREAST
176.0-176.9	KAPOSI'S SARCOMA SKIN - KAPOSI'S SARCOMA UNSPECIFIED SITE
179	MALIGNANT NEOPLASM OF UTERUS-PART UNS
182.0	MALIGNANT NEOPLASM OF CORPUS UTERI EXCEPT ISTHMUS
182.1	MALIGNANT NEOPLASM OF ISTHMUS
182.8	MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF BODY OF UTERUS
183.0	MALIGNANT NEOPLASM OF OVARY
183.2-183.5	MALIGNANT NEOPLASM OF FALLOPIAN TUBE - MALIGNANT NEOPLASM OF ROUND LIGAMENT OF UTERUS
183.8	MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES OF UTERINE ADNEXA
183.9	MALIGNANT NEOPLASM OF UTERINE ADNEXA UNSPECIFIED SITE
200.70-200.78	LARGE CELL LYMPHOMA, UNSPECIFIED SITE, EXTRANODAL AND SOLID ORGAN SITES - LARGE CELL LYMPHOMA, LYMPH NODES OF MULTIPLE SITES
200.80-200.88	OTHER NAMED VARIANTS OF LYMPHOSARCOMA AND RETICULOSARCOMA UNSPECIFIED SITE - OTHER NAMED VARIANTS OF LYMPHOSARCOMA AND RETICULOSARCOMA INVOLVING LYMPH NODES OF MULTIPLE SITES
202.10-202.18	MYCOSIS FUNGOIDES UNSPECIFIED SITE - MYCOSIS FUNGOIDES INVOLVING LYMPH NODES OF MULTIPLE SITES
202.20-202.28	SEZARY'S DISEASE UNSPECIFIED SITE - SEZARY'S DISEASE INVOLVING LYMPH NODES OF MULTIPLE SITES
202.80-202.88	OTHER MALIGNANT LYMPHOMAS UNSPECIFIED SITE - OTHER MALIGNANT LYMPHOMAS INVOLVING LYMPH NODES OF MULTIPLE SITES
203.00-203.02	MULTIPLE MYELOMA, WITHOUT MENTION OF HAVING ACHIEVED REMISSION - MULTIPLE MYELOMA, IN RELAPSE
203.10	PLASMA CELL LEUKEMIA, WITHOUT MENTION OF HAVING ACHIEVED REMISSION

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**Background:**

Doxorubicin lipid complex is in a class of medications called anthracyclines. It works by slowing or stopping the growth of cancer cells in your body. Anthracyclines are notorious for causing cardiotoxicity. Anthracycline has three mechanisms of action:

1. Inhibits DNA and RNA synthesis by intercalating between base pairs of the DNA/RNA strand, thus preventing the replication of rapidly-growing cancer cells.
2. Inhibits topoisomerase II enzyme, preventing the relaxing of supercoiled DNA and thus blocking DNA transcription and replication. Some sources say that topo II inhibitors prevent topo II from turning over which is needed for dissociation of topo II from its nucleic acid substrate. In other words, topo II stabilizes the topo II complex after it has broken the DNA chain. This leads to topo II mediated DNA-cleavage, producing DNA breaks. The binding of topo II inhibitor prevents DNA repair by ligase.
3. Creates iron-mediated free oxygen radicals that damage the DNA and cell membranes.



**Black Box Warning:**

**WARNING: INFUSION REACTIONS, MYELOSUPPRESSION, CARDIOTOXICITY, LIVER IMPAIRMENT, ACCIDENTAL SUBSTITUTION**

- 1. The use of DOXIL (doxorubicin HCl liposome injection) may lead to cardiac toxicity. Myocardial damage may lead to congestive heart failure and may occur as the total cumulative dose of doxorubicin HCl approaches 550 mg/m<sup>2</sup>. In a clinical study in patients with advanced breast cancer, 250 patients received DOXIL at a starting dose of 50 mg/m<sup>2</sup> every 4 weeks. At all cumulative anthracycline doses between 450-500 mg/m<sup>2</sup> or between 500-550 mg/m<sup>2</sup>, the risk of cardiac toxicity for patients treated with DOXIL was 11%. Prior use of other anthracyclines or anthracenediones should be included in calculations of total cumulative dosage. Cardiac toxicity may also occur at lower cumulative doses in patients with prior mediastinal irradiation or who are receiving concurrent cyclophosphamide therapy.**
- 2. Acute infusion-related reactions including, but not limited to, flushing, shortness of breath, facial swelling, headache, chills, back pain, tightness in the chest or throat, and/or hypotension have occurred in up to 10% of patients treated with DOXIL. In most patients, these reactions resolve over the course of several hours to a day once the infusion is terminated. In some patients, the reaction has resolved with slowing of the infusion rate. Serious and sometimes lifethreatening or fatal allergic/anaphylactoid-like infusion reactions have been reported. Medications to treat such reactions, as well as emergency equipment, should be available for immediate use. DOXIL should be administered at an initial rate of 1 mg/min to minimize the risk of infusion reactions.**
- 3. Severe myelosuppression may occur.**
- 4. Dosage should be reduced in patients with impaired hepatic function.**
- 5. Accidental substitution of DOXIL for doxorubicin HCl has resulted in severe side effects. DOXIL should not be substituted for doxorubicin HCl on a mg per mg basis.**

**Definitions:**

HCCPS Code—Healthcare Common Procedure Coding System - A system of letter and number codes assigned to procedures, medications, supplies and equipment used for pricing and billing.



ICD-9 Code—International Classification of Disease, 9<sup>th</sup> edition. A standardized classification of disease, injuries, and causes of death, by etiology and anatomic localization and codified into a 6-digit number, which allows clinicians, statisticians, politicians, health planners and others to speak a common language, both US and internationally.

#### References:

1. Doxil [package insert]. Raritan, NJ: Centocor Ortho Biotech Products, L.P.; March 2011. Available at: [http://www.doxil.com/assets/DOXIL\\_PI\\_Booklet.pdf](http://www.doxil.com/assets/DOXIL_PI_Booklet.pdf). June 7, 2012.
2. The NCCN Drugs & Biologics Compendium™ © 2010 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed May 23, 2012.
3. Local Coverage Article for Drugs and Biologicals – Chemotherapeutic Agents (A48896) (R4). Available at: [http://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=48896&ver=89&ContrId=213&ContrVer=1&CtrctrSelected=213\\*1&Date=01%2f01%2f2013&DocId=A48896&bc=hAAAAAgAEAAAAA%3d%3d&](http://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=48896&ver=89&ContrId=213&ContrVer=1&CtrctrSelected=213*1&Date=01%2f01%2f2013&DocId=A48896&bc=hAAAAAgAEAAAAA%3d%3d&). Accessed June 4, 2014.
4. Micromedex® 2.0 Doxil. Available at: [http://www.thomsonhc.com/micromedex2/librarian/ND\\_T/evidencexpert/ND\\_PR/evidencexpert/CS/E283D3/ND\\_AppProduct/evidencexpert/DUPLICATIONSHIELDSYNC/AFD97B/ND\\_PG/evidencexpert/ND\\_B/evidencexpert/ND\\_P/evidencexpert/PFActionId/evidencexpert.DisplayDrugpointDocument?docId=924052&contentSetId=100&title=Doxorubicin+Hydrochloride+Liposome&servicesTitle=Doxorubicin+Hydrochloride+Liposome&topicId=dosingAndIndicationsSection&subtopicId=nonfdaSection..](http://www.thomsonhc.com/micromedex2/librarian/ND_T/evidencexpert/ND_PR/evidencexpert/CS/E283D3/ND_AppProduct/evidencexpert/DUPLICATIONSHIELDSYNC/AFD97B/ND_PG/evidencexpert/ND_B/evidencexpert/ND_P/evidencexpert/PFActionId/evidencexpert.DisplayDrugpointDocument?docId=924052&contentSetId=100&title=Doxorubicin+Hydrochloride+Liposome&servicesTitle=Doxorubicin+Hydrochloride+Liposome&topicId=dosingAndIndicationsSection&subtopicId=nonfdaSection..) Accessed 6-7-12

#### Document History:

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