Doxorubicin HCl Liposome (Doxil®)

Prior Authorization Drug Coverage Policy

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Lines of Business: Commercial
Policy type: Prior Authorization

This Drug Coverage Policy provides parameters for the coverage of doxorubicin HCl liposome. Consideration of medically necessary indications are based upon U.S. Food and Drug Administration (FDA) indications, recommended uses within the Centers of Medicare & Medicaid Services (CMS) five recognized compendia, including the National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium (Category 1 or 2A recommendations), and peer-reviewed scientific literature eligible for coverage according to the CMS, Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 titled, "Off-Label Use of Anti-Cancer Drugs and Biologics." This policy evaluates whether the drug therapy is proven to be effective based on published evidence-based medicine.

Drug Description[1]

The active ingredient of Doxil® is doxorubicin HCl. 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® is doxorubicin HCl encapsulated in long-circulating Stealth® liposomes. Liposomes are microscopic vesicles composed of a phospholipid bilayer that are capable of encapsulating active drugs. The Stealth® liposomes of Doxil® are formulated with surface-bound methoxypolyethylene glycol (MPEG), a process often referred to as pegylation, to protect liposomes from detection by the mononuclear phagocyte system (MPS) and to increase blood circulation time.

Stealth® liposomes have a half-life of approximately 55 hours in humans. They are stable in blood, and direct measurement of liposomal doxorubicin shows that at least 90% of the drug (the assay used cannot quantify less than 5-10% free doxorubicin) remains liposome-encapsulated during circulation.

It is hypothesized that because of their small size (ca. 100 nm) and persistence in the circulation, the pegylated Doxil® liposomes are able to penetrate the altered and often compromised vasculature of tumors. This hypothesis is supported by studies using colloidal gold-containing Stealth® liposomes, which can be visualized microscopically. Evidence of penetration of Stealth®

liposomes from blood vessels and their entry and accumulation in tumors has been seen in mice with C-26 colon carcinoma tumors and in transgenic mice with Kaposi's sarcoma-like lesions. Once the Stealth® liposomes distribute to the tissue compartment, the encapsulated doxorubicin HCl becomes available. The exact mechanism of release is not understood.

FDA Indications[1]

Doxorubicin HCl liposome is FDA indicated for the following:

- Treatment of patients with ovarian cancer whose disease has progressed or recurred after platinum-based chemotherapy.
- Treatment of AIDS-related Kaposi's sarcoma in patients with disease that has progressed on prior combination chemotherapy or in patients who are intolerant to such therapy.
    - The treatment of patients with AIDS-related Kaposi's sarcoma is based on objective tumor response rates. No results are available from controlled trials that demonstrate a clinical benefit resulting from this treatment, such as improvement in disease-related symptoms or increased survival.
- In combination with bortezomib for the treatment of patients with multiple myeloma who have not previously received bortezomib and have received at least one prior therapy.

NCCN Compendium Supported Indications[2]

- B-Cell Lymphomas
- Breast Cancer
- Hodgkin Lymphoma
- Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer
- Primary Cutaneous Lymphomas
- Soft Tissue Sarcoma
- T-Cell Lymphomas
- Uterine Neoplasms

Coverage Determinations[1,2]

Doxorubicin HCl liposome will require prior authorization. This agent is considered medically necessary for the following oncology indications if all criteria below are met.

Platinum-Sensitive Ovarian Cancer

- The member has a diagnosis of ovarian cancer **AND**
- The member meets one of the following:
    - The member has chemotherapy-naïve, advanced disease **OR**
    - The member has platinum-sensitive, recurrent/relapsed disease (progression or recurrence more than 6 months after first- or second-line platinum and taxane-based therapies) **AND**

- Doxorubicin HCl liposome will be used in combination with carboplatin (for neoadjuvant, adjuvant, first-line or subsequent therapy) with or without bevacizumab (for subsequent therapy)

Recommended dosage: 30 mg/m^2 IV every 28 days

Platinum-Resistant Ovarian Cancer

- The member has a diagnosis of ovarian cancer **AND**
- The member has platinum-resistant, recurrent disease (progression or recurrence within 6 months after completion of platinum-based therapy) **AND**
- Doxorubicin HCl liposome will be used as monotherapy or in combination with bevacizumab

Recommended dosage: 40 to 50 mg/m^2 IV every 28 days

AIDS-Related Kaposi's Sarcoma (AIDS-KS)

- The member has a diagnosis of AIDS-KS **AND**
- The member has advanced disease **AND**
- The member meets one of the following:
  - Progressed on prior combination therapy **OR**
  - Is intolerant to combination therapy **AND**
- Doxorubicin HCl liposome will be used as monotherapy

Recommended dosage: 20 mg/m^2 IV every 14-21 days for 6 cycles

Multiple Myeloma (MM)

- The member has a diagnosis of MM **AND**
- The member meets all of the following:
  - Has received at least one prior therapy **AND**
  - Is bortezomib-naïve **AND**
  - Has relapsed or refractory disease **AND**
- Doxorubicin HCl liposome will be used in combination with bortezomib.

Recommended dosage: 30 mg/m^2 IV on day 4 every 21 days for 6 cycles

Breast Cancer

- The member has a diagnosis of recurrent or metastatic breast cancer **AND**
- The member has disease that is:
  - HER2-negative **AND**
  - Hormone receptor-negative **OR**
  - Hormone receptor-positive with visceral involvement **OR**
  - Hormone receptor-positive refractory to endocrine therapy **AND**
- Doxorubicin HCl liposome will be used as monotherapy

Recommended dosage: 40 to 50 mg/m^2 IV every 28 days

Cutaneous T-Cell Lymphoma (CTCL)

- The member has a diagnosis of mycosis fungoides **AND**
- The member has disease that is:
  - Advanced (stage IIA, IVA, or IVB) **AND**
  - Refractory or recurrent disease after 2 or more previous therapies **AND**
- Doxorubicin HCl liposome will be used as monotherapy

Recommended dosage: 20 mg/m^2 IV on days 1 and 15 every 28 days for 6 cycles

Diffuse Large B-Cell Lymphoma (DLBCL)

- The member has a diagnosis of DLBCL (including histologic transformations to DLBCL) **AND**
- The member has disease that is:
  - Previously untreated **AND**
  - Low-grade **OR**
  - Low/intermediate risk **AND**
- The member meets one of the following:
  - Frail and elderly **OR**
  - Has poor left ventricular ejection fraction **AND**
- Doxorubicin HCl liposome will be used in combination with rituximab (if CD20-positive), cyclophosphamide, vincristine, and prednisone for first-line treatment

Recommended dosage: 30 mg/m^2 IV every 21 days for 6 cycles

Hodgkin Lymphoma (HL)

- The member has a diagnosis of relapsed or refractory disease HL **AND**
- Doxorubicin HCl liposome will be used as salvage therapy in combination with gemcitabine and vinorelbine **AND**

Recommended dosage: 15 mg/m^2 (transplant-naïve) or 10 mg/m^2 (prior transplant) IV on days 1 and 8 every 21 days for 6 cycles

All indications:

- Doxorubicin HCl liposome will be approved through clinical review for up to a 6-month duration.

Coverage Limitations

Treatment with doxorubicin HCl liposome is not considered medically necessary for members with the following concomitant conditions:

- The member has experienced disease progression on or after doxorubicin HCl liposome.
- The member has reached the maximum lifetime cumulative anthracycline dose.
- The member has preexisting cardiac conditions that makes doxorubicin HCl liposome an unsuitable treatment option.
- Indications not supported by NCCN category 2A or higher recommendations may not be considered medically necessary

Contraindications/Warnings/Precautions[1]

- Contraindications:
    - Hypersensitivity reactions to a conventional formulation of doxorubicin HCl or the components of Doxil®
    - Nursing Mothers
- Warnings/Precautions:
    - Hand-Foot Syndrome
    - Radiation Recall Reaction

For specific recommendations on contraindications, warnings and precautions, patient monitoring, and on dose adjustments and discontinuation, please refer to the current prescribing information.

Billing

- Description: inj., doxorubicin HCl liposome, 1 mg
    - HCPCS: Q2049, Q2050

Disclaimer

Drug Coverage Policies are developed as needed, regularly reviewed, updated at least annually, and are subject to change. Other policies and coverage determination guidelines may apply. Federal and state regulatory requirements and member specific benefit plan documents, if applicable, must be reviewed prior to this Drug Coverage Policy. This Drug Coverage Policy is for informational purposes only and does not constitute medical advice or dictate how providers should practice medicine. This policy should not be reproduced, stored in a retrieval system, or altered from its original form without written permission from Oncology Analytics, Inc.

References

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